Evidence Synthesis Program

# Self-management of Epilepsy: A Systematic Review

Prepared for:
Department of Veterans Affairs
Veterans Health Administration
Health Services Research & Development Service
Washington, DC 20420

Prepared by:
Evidence Synthesis Program (ESP) Center
Durham Veterans Affairs Healthcare System
Durham, NC
John W. Williams, Jr., MD, MHSc, Director

Authors:

Principal Investigator:
Matthew W. Luedke, MD
Dan V. Blalock, PhD, MA
John W. Williams, Jr., MD, MHS

Co-Investigators:
Allison A. Lewinski, PhD, MPH, RN
Abigail Shapiro, MSPH
Connor Drake, MPA
Jeffrey D. Lewis, PhD, MD
Karen M. Goldstein, MD, MSPH
Aatif M. Husain, MD
Saurabh R. Sinha, MD, PhD
Tung T. Tran, MD
Adelaide M. Gordon, MPH
Andrzej S. Kosinski, PhD
Hayden B Bosworth, PhD

Research Associates:
Avishek Nagi, MS
Robyn E. Fortman, BA
Christiana Oshotse

Medical Editor:
Liz Wing, MA

VA
U.S. Department of Veterans Affairs
Veterans Health Administration
*Health Services Research & Development Service*

# PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program is comprised of four ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program and Cochrane Collaboration. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, and interface with stakeholders. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee comprised of health system leadership and researchers. The program solicits nominations for review topics several times a year via the program website.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at Nicole.Floyd@va.gov.

**Recommended citation:** Luedke MW, Blalock DV, Lewinski AA, Shapiro A, Drake C, Lewis JD, Goldstein KM, Husain AM, Gierisch JM, Sinha SR, Tran TT, Gordon AM, Kosinski AS, Bosworth HB, Van Noord M, Williams JW Jr. Self-management of Epilepsy. VA ESP Project #09-009; 2019. Posted final reports are located on the ESP search page.

This report is based on research conducted by the Evidence Synthesis Program (ESP) Center located at the **Durham VA Medical Center, Durham, NC**, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

# ACKNOWLEDGMENTS

This topic was developed in response to a nomination by Glenn Graham, Deputy National Director of Neurology, and John Hixson, Associate Professor of Neurology, for the purpose of identifying the current evidence base and its quality to support the use of self-management programs aimed at patients with epilepsy; identifying the program components that contribute most to effectiveness; and identifying potential barriers in the adoption of these programs within the VHA system. The scope was further developed with input from the topic nominators (*ie*, Operational Partners), the ESP Coordinating Center, the review team, and the Technical Expert Panel (TEP).

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

The authors gratefully acknowledge the following individuals for their contributions to this project.

## Operational Partners

Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend TEP participants; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on the draft report; and provide consultation on strategies for dissemination of the report to field and relevant groups.

Glenn Graham, MD, PhD
Deputy National Director of Neurology

John Hixson, MD
Associate Professor of Neurology
Epilepsy Center of Excellence (ECoE), San Francisco VA Medical Center
Neurology Program Office, VHA

## Technical Expert Panel

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress.

Jennifer Patterson, PhD
Senior Whole Health Consultant
Office of Patient Centered Care & Cultural Transformation
VA Sierra Nevada Health Care System
Reno, Nevada

Paul Rutecki, MD
Neurology Service Chief
William S. Middleton Veterans Hospital
Madison, Wisconsin
National Director VA Epilepsy Centers of Excellence
Professor of Neurology and Neurosurgery
University of Wisconsin-Madison

## Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence. Peer reviewers must disclose any relevant financial or nonfinancial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center and the ESP Center work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

# TABLE OF CONTENTS

**TABLES**

## FIGURES

# EXECUTIVE SUMMARY

## INTRODUCTION

Epilepsy affects about 50 million people worldwide. In the Veterans Health Administration (VHA), an estimated 79,576 Veterans were treated for epilepsy in 2016. Seizure control and medication adherence are common challenges among patients; decreased health care literacy, poor social support, burdensome side effects, low socioeconomic status, and co-occurring psychiatric disorders are all associated with lower medication adherence. Patient self-management behaviors are important to the management of epilepsy, as decreased patient participation in treatment regimens is a major cause of breakthrough seizures, leading to increased hospital utilization and mortality.

In 2003, the Institute of Medicine defined self-management support as “the systematic provision of education and supportive interventions by health care staff to increase patients’ skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support.” In Veterans Affairs (VA), self-management has an established role in the management of chronic conditions, such as diabetes mellitus, chronic obstructive pulmonary disease, and depressive disorders.

For patients with epilepsy, improved self-management skills could improve self-efficacy, medication adherence, avoidance of seizure triggers, and improve patient and family knowledge about when to seek urgent medical care. A Cochrane review that included literature published through December 2013 evaluated self-management strategies for adults with epilepsy. The review identified only 4 trials and concluded that self-management education has some evidence of benefit but did not find clear evidence of substantially improved outcomes for adults with epilepsy. Prior systematic reviews on this topic were inadequate for the needs of our stakeholders because they do not include recent important studies and did not adequately consider components such as peer support, which has particular relevance to Veterans. This review will address these gaps in evidence, synthesize the current evidence on self-management programs for patients with epilepsy, and identify potential barriers in the adoption of these programs within the VHA system.

At the request of the VA National Neurology Program Office in the Office of Specialty Care Services, we conducted a systematic review and meta-analysis to address the following key questions (KQ):

**KQ 1:** For adults with epilepsy, what are the most commonly employed components of self-management interventions evaluated in comparative studies?

**KQ 2:** What are the effects of self-management interventions on self-management skills and self-efficacy, clinical outcomes, and health care utilization?

**KQ 3:** What are the identified facilitators and barriers that impact the adoption of self-management interventions in large-scale health systems such as the VHA?

## METHODS

We developed and followed a standard protocol for this review in collaboration with operational partners and a Technical Expert Panel (PROSPERO registration number CRD42018098604).

### Data Sources and Searches

We searched MEDLINE® (via PubMed®), PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL), and CINAHL from inception through April 13, 2018, and updated the MEDLINE search on October 31, 2018. We also examined the bibliographies of recent reviews for additional relevant studies.

### Study Selection

In brief, the major eligibility criteria were randomized or quasi-experimental studies that enrolled adults with epilepsy, evaluated self-management interventions, and reported a relevant clinical, process, or economic outcome. For KQ 3, we also included additional observational designs and qualitative studies addressing facilitators or barriers to adoption or implementation. Self-management interventions were defined operationally as those that aimed to equip patients with skills to actively participate and take responsibility in the management of epilepsy in order to function optimally through at least knowledge acquisition and a combination of 1 or more of the following: stimulation of independent sign/symptom monitoring; medication management; enhancing problem-solving and decision-making skills for epilepsy treatment management; safety promotion (*eg*, driving); and changing health behaviors (*eg*, stress management, sleep, substance use). Using these prespecified inclusion/exclusion criteria, investigators and the DistillerSR Artificial Intelligence tool evaluated titles and abstracts to identify potentially eligible studies. Studies that met all eligibility criteria at full-text review were included for data abstraction.

### Data Abstraction and Quality Assessment

Key characteristics abstracted were patient descriptors (*eg*, age, duration of epilepsy), intervention characteristics (*eg*, self-management components, delivery modality, duration/intensity), comparator, and outcomes. For studies relevant to KQ 3, we abstracted barriers (*ie*, description of themes or factors that impeded the use and implementation of the intervention as reported in the study's results and/or findings sections) and facilitators (*ie*, description of themes or factors that aided the use of the intervention as reported in the study's results and/or findings sections) to the implementation of self-management interventions (as distinct from barriers and facilitators of an individual engaging in self-management behaviors).

For KQ 1 and KQ 2 studies, we assessed risk of bias (ROB) using the Effective Practice and Organization of Care (EPOC) guidance. For KQ 3 studies, we used ROB appraisals customized to the specific study design.

### Data Synthesis and Analysis

We described the included studies using summary tables and graphical displays. We computed summary effects (*ie*, meta-analysis) when studies were conceptually homogeneous and there were at least 3 studies with the same outcome. When quantitative synthesis was feasible, we combined outcomes using random-effects models and computed summary effects using the standardized mean difference. Analyses were stratified by study design (randomized vs nonrandomized) and by intervention category. When quantitative synthesis was not feasible, we analyzed the data narratively.

We analyzed potential reasons for inconsistency in treatment effects across studies by evaluating differences in the study population, intervention, comparator, and outcome definitions. Confidence of evidence (COE) was assessed for outcomes critical to decision making using the approach described by the Grading of Recommendations Assessment, Development and Evaluation working group (GRADE).

For KQ 3, 2 co-investigators (AAL, AS) with experience in qualitative methodology led the abstraction and analysis of data collected. We analyzed the data using thematic synthesis and the framework method. First, we identified the respondent (*eg*, the patient with epilepsy, caregiver, or health care clinician) for each facilitator and barrier. Then, we created an *a priori* framework that included barriers and facilitators as reported at 1 of 3 levels (*eg*, person, program, site/system) adapted from ecological models of health behavior. The creation and identification of codes and themes was iterative; to ensure rigor and validity of these findings, we independently coded and developed themes and then discussed theme development and identification until we reached agreement between the 2 researchers.

## RESULTS

### Results of Literature Search

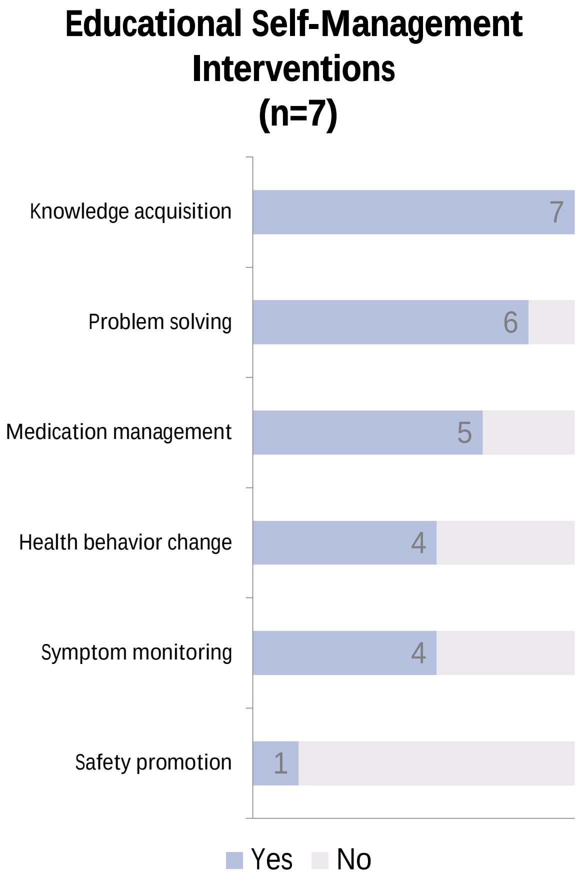
The literature search identified 2,543 citations, of which 161 were reviewed at the full-text stage. Fifteen articles relevant to KQs 1 and 2 were retained for data abstraction, of which 13 were randomized and 2 were nonrandomized; one enrolled Veterans. Because some studies had more than 1 active intervention arm, a total of 18 intervention arms are described across the 15 studies. Thirteen articles relevant to KQ 3 were retained for data abstraction.

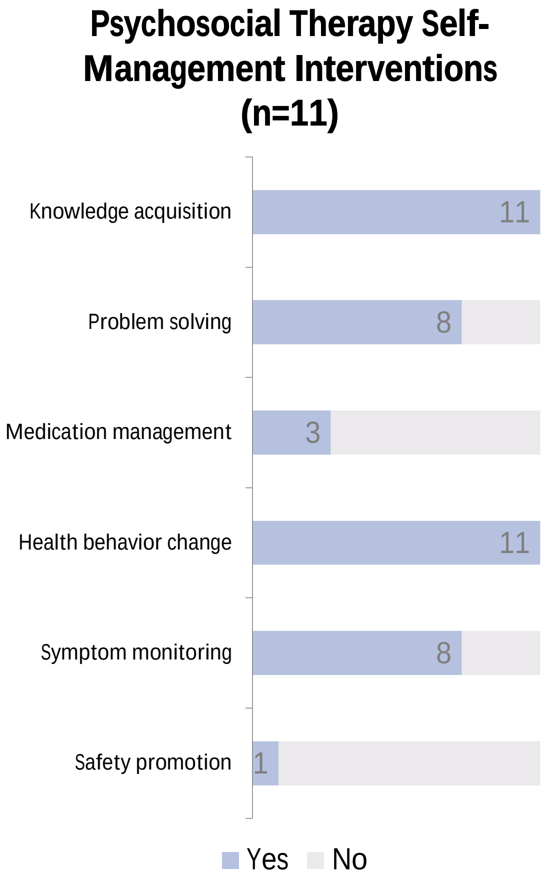
### Summary of Results for Key Questions

#### *KQ 1*

Self-management interventions for adults with epilepsy used 2 main approaches: educational interventions with content created specifically for patients with epilepsy (n=7 studies, 7 intervention arms) and psychosocial therapy interventions (*eg*, cognitive behavioral therapy, problem solving therapy, progressive muscle relaxation) established for other conditions and adapted for patients with epilepsy (n=8 studies, 11 intervention arms). Intervention approaches most commonly addressed education—implicitly or explicitly—as well as stimulation of independent sign/symptom monitoring; enhancing problem-solving and decision-making skills for medical treatment management; and changing physical activity, dietary, and/or smoking behaviors. These intervention components were delivered during 4-41 hours of training over a broad range of times anywhere from 2 days to 3 years. Peer support was only provided explicitly in 1 study, although 3 studies incorporated peers as group leaders. Goal-setting was present in 8 studies.

### Self-management Components Addressed in Interventions





### *KQ 2*

Among the interventions that used an educational approach, the use of self-management practices may have improved among people with epilepsy, although the certainty of evidence (COE) is low, and there was no effect on overall quality of life (low COE) or seizure rate (moderate COE). Similarly, there was no overall effect on self-efficacy, social function, or medication adherence. However, a stakeholder-informed, group-based intervention delivered to patients at high risk for poor outcomes (including Veterans) showed moderate benefit for quality of life and self-efficacy. Among interventions that used a psychosocial therapy approach, there was a positive effect on overall quality of life (low COE) but no benefit on seizure rates (low COE), and there was insufficient evidence to determine effects on self-management practices. Additionally, sparse evidence suggested some benefit on self-efficacy; there were inconsistent effects on social function and limited data for no effect on medication adherence. COE was evaluated only for primary outcomes. One study of an intervention using a group-based intervention in high-risk patients found no effect on the combined outcome of emergency department visits and hospitalization. No study reported effects on workplace productivity or employment status. Only one study reported enrolling Veterans.

### Certainty of Evidence for Primary Outcomes of Self-management Interventions for Patients with Epilepsy

| Outcome | Number of Studies (Patients) | Findings | Certainty of Evidence (Rationale) |
|---|---|---|---|
| *Educational Self-management Interventions* | | | |
| Epilepsy self-management | 4 randomized (569) | SMD 0.52 higher<br>(0 to 1.04 higher) | **Low certainty** of improved self-management |
| Quality of life | 4 randomized (492)<br>1 nonrandomized (747) | SMD 0.17<br>(0.57 lower to 0.91 higher)<br>MD 0.5<br>(6.4 lower to 7.4 higher) | **Low certainty** for no effect |
| Seizure rates | 4 randomized (787) | SMD 0.00<br>(-0.3 lower to 0.04 higher) | **Moderate certainty** for no effect |
| *Psychosocial Therapy Self-management Interventions* | | | |
| Epilepsy self-management | None | Not applicable | **Insufficient** |
| Quality of life | 3 randomized (187) | MD 6.64 higher<br>(2.51 to 10.77 higher) | **Low certainty** for improved quality of life |
| Seizure rates | 3 randomized (106) | SMD range from 0.06 to 0.47 | **Low certainty** for no clinically important improvement |

Abbreviations: MD=mean difference; NR=not reported; SMD=standardized mean difference; ROB=risk of bias

### *KQ 3*

Thematic synthesis of the abstracted data identified 5 themes across all KQ 3 studies that could be applied conceptually to facilitators and barriers. The presence of facilitators of epilepsy self-management interventions at any level (*ie*, person, program, site/system) was noted in 11 studies. Two studies did not include any relevant facilitators. The presence of barriers to epilepsy self-management interventions at any level was noted in 11 studies. Two studies did not include any relevant barriers.

| Theme | Definition |
|---|---|
| **Relevance** | Relevance of intervention content or topics that facilitate the acquisition of self-management skills in patients with epilepsy |
| **Personalization** | Intervention components that account for the individual social, physical, and environmental characteristics of the patient |
| **Intervention components** | Components and dosing of the intervention |
| **Technology considerations** | Considerations that account for patient’s use, familiarity with, and ownership of technology (*eg*, computers, laptops, mobile phones) |
| **Clinician interventionist** | Role and preparation of individual who leads the intervention, engages with the patient, and provides self-management education and/or support to the patient |

Involving patients with epilepsy in the development of interventions may facilitate implementation by ensuring that the self-management content is relevant to people living with the condition. Including customizable intervention content to allow for tailoring to each individual patient may facilitate implementation. Patients may have cognitive limitations that present a barrier to intervention engagement and adherence. Technology use for self-management is highly dependent on individual characteristics such as familiarity and ownership of technological devices (*eg*, mobile phones, computers). The role of the clinician (*ie*, the individual who interacts with the patient to provide self-management education and support) is important to the implementation of the intervention. The clinician should be appropriately trained, have the duties of the intervention incorporated into their dedicated clinical time, and be provided with clearly written standardized protocols that articulate the clinician interventionist's role in the intervention. No studies directly addressed facilitators and barriers to implementing and adopting self-management interventions for patients with epilepsy in the VHA or other large health systems. No studies intentionally enrolled Veterans with epilepsy.

# DISCUSSION

## Key Findings

We evaluated self-management interventions for patients with epilepsy, examining effects on a range of outcomes of importance to patients, clinicians, and policymakers. Our review is unique in its use of a standard definition for self-management, focus on high-quality study designs, and rigorous analysis of studies that address facilitators and barriers to implementation and adoption of self-management interventions. We identified 15 studies addressing the effects of self-management and 13 that addressed implementation and adoption. Only 1 specifically included Veterans. We identified 2 broad categories for self-management interventions: educationally focused interventions created for patients with epilepsy, and psychosocial therapies such as cognitive behavioral therapy (CBT) that were adapted for people with epilepsy. We found limited evidence for benefit on selected primary or secondary outcomes. Educational self-management interventions may improve the use of self-management practices, and quality of life may improve with therapy-based self-management approaches. There was low to moderate certainty of no improvement in seizure rates across self-management interventions. Sparse evidence suggested possible benefit of psychosocial therapy interventions on self-efficacy. Effects on employment and health care utilization were not reported.

Studies of barriers and facilitators to implementation and adoption of epilepsy self-management interventions addressed factors primarily at the patient level or program level. No studies directly addressed implementation and adoption issues for large health systems such as the VHA. Important themes that could inform the development, implementation, and/or adoption of future self-management interventions included the desire of patients with epilepsy to be involved in the development of intervention content, recognition that cognitive limitations may affect engagement and adherence, and the need for clinician interventionists who are appropriately trained to provide self-management interventions and whose job function specifically includes this role.

## Applicability

Only 1 of the included studies specifically enrolled Veterans. However, we limited eligibility to studies conducted in OECD countries, which improves applicability to the VHA. All intervention studies were conducted in North America, Europe, or Australia. Identified studies included predominantly white samples, and mid-life patients (median age 41 in contrast to the >50% of Veterans with epilepsy who are 65 years of age or older). Although this approach improved applicability of findings to Veterans, it means that potentially relevant studies conducted in non-OECD countries were excluded.

## Research Gaps/Future Research

In brief, research is needed with patients who are earlier in their course of illness, and on barriers and facilitators to adoption of self-management interventions in large health systems and with Veterans. Interventions are needed that incorporate patient, caregiver, and clinician interventionist input into the self-management content and delivery design. Self-management programs should account for potential cognitive limitations, incorporate peer support, address other barriers to engagement and adherence, and address the composition of the intervention team as well as the role of technology.

Research is needed on outcomes most valued by patients with epilepsy, and how to best measure these outcomes. Self-management skills can take time to master and may take longer for patients with cognitive difficulty. Consensus, or research, on the time required to acquire self-management skills, and for those skills to affect clinical outcomes, should inform the timing of outcome assessments. Few studies have examined interventions delivered outside of clinical settings. Future research should determine the preferred location for a self-management program for patients with epilepsy and their caregivers.

## Conclusions

Epilepsy is one of the most common chronic neurological conditions, with the potential to generate significant morbidity, impaired quality of life, socioeconomic decline, and high health care costs. Self-management is essential for patients who live with a chronic disease, and the VHA and other health systems are interested in offering self-management training to patients with epilepsy. In our protocol-based review, we found that tested interventions broke down into 2 categories: educational and psychosocial therapy interventions. These self-management interventions showed clinically important benefit for only a limited number of outcomes, but the confidence in these findings was mostly low. Further, there is unexplained variability in the effect of education interventions on quality of life and self-efficacy. Findings on facilitators and barriers to the implementation were stronger and point to a clearer path to the design and adoption of self-management interventions, including factors of patient personalization, information delivery, use of technology, and intervention personnel. Future research should be designed to address these implementation issues, and should include standardized outcome measures prioritized by patients and other stakeholders and Veteran populations.

# ABBREVIATIONS TABLE

| | |
|---|---|
| AED | Antiepileptic drug |
| CBT | Cognitive behavioral therapy |
| CI | Confidence interval |
| CINAHL | Cumulative Index to Nursing and Allied Health Literature |
| COE | Certainty of evidence |
| ECoE | Epilepsy Centers of Excellence |
| ESES | Epilepsy Self-Efficacy Scale |
| ESMS | Epilepsy Self-Management Scale |
| ESP | Evidence Synthesis Program |
| HSR&D | Health Services Research & Development |
| IOM | Institute of Medicine |
| LTC | Long-term condition |
| MD | Mean difference |
| MeSH | Medical Subject Heading |
| MMAT | Mixed Methods Appraisal Tool |
| MMSE | Mini-Mental State Examination |
| MOSES | Modular Service Package for Epilepsy |
| OECD | Organization for Economic Cooperation and Development |
| PACES | Program for Active Consumer Engagement in Epilepsy |
| PACT | Patient-Aligned Care Team |
| PICOTS | Population, intervention, comparator, outcome, timing, and setting |
| PMR | Progressive muscle relaxation |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta Analyses |
| PST | Problem-solving therapy |
| QOL | Quality of life |
| QUERI | Quality Enhancement Research Initiative |
| QUIET | Quality Indicators in Epilepsy Treatment tool |
| SMD | Standardized mean difference |
| ROB | Risk of bias |
| VA | Veterans Affairs |
| VHA | Veterans Health Administration |

# EVIDENCE REPORT

## INTRODUCTION

Epilepsy affects about 50 million people worldwide,[1] with the highest rates in children and older adults. In VHA, an estimated 79,576 Veterans were treated for epilepsy in 2016; almost 50% were 65 years of age or older. In the Veteran population, there is a significant association with prior traumatic brain injury; this is of particular importance to Veterans serving in Operation Iraqi Freedom and Operation Enduring Freedom.[2]

Epilepsy may diminish quality of life even when seizures are controlled.[3-5] Patients with epilepsy are at greater risk for mood disorders and have higher rates of injury and premature death than the general population. Sex-specific issues can complicate epilepsy care, such as interactions between antiepileptic drugs (AEDs) and contraceptive agents or management of teratogenic AEDs during pregnancy.[6,7] Patients often face the challenges of low socioeconomic status along with high levels of perceived social stigma, creating financial and social barriers to care.[8] Seizure control and medication adherence are common challenges among patients; decreased health care literacy, poor social support, burdensome side effects, low socioeconomic status, and co-occurring psychiatric disorders are all associated with lower medication adherence.[9-12] Further, some epilepsies are associated with cognitive impairment or impulse-control issues, further complicating care plans. Patient self-management behaviors are very important to the management of epilepsy, as decreased patient participation in treatment regimens is a major cause of breakthrough seizures, leading to increased hospital utilization and mortality.[13,14]

In 2003, the Institute of Medicine defined self-management support as “the systematic provision of education and supportive interventions by health care staff to increase patients’ skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support.”[15] Self-management support is a core component of care delivery models[16-18] developed to improve chronic disease care, such as the patient-centered medical home,[19] and is a requirement for participation in some Medicare alternative payment programs.[20] In VA, self-management has an established role in the management of chronic conditions and is a core component of programs such as primary care–mental health integration and patient-aligned care teams.

Systematic reviews have shown that self-management support for patients with chronic illness improves symptoms and role function, but these positive effects are influenced by the type of chronic illness and self-management skills taught.[21-23] Further, the effectiveness of self-management may be influenced by co-occurring conditions such as traumatic brain injury or depressive disorders, and by levels of education or health literacy. For patients with epilepsy, improved self-management skills could improve self-efficacy (an individual’s belief in his or her innate ability to achieve goals), medication adherence, avoidance of seizure triggers, and improve patient and family knowledge about when to seek urgent medical care. This represents a more holistic approach to chronic illness care than strategies such as patient education or reminders that focus solely on medication adherence. Self-management interventions hold promise for patients with epilepsy, although cognitive impairment and psychiatric disease that are frequently comorbid with epilepsy, along with the paroxysmal nature of seizures, may attenuate the effects of these interventions. A Cochrane review that included literature published through December 2013 evaluated self-management strategies for adults with epilepsy.[24] The review identified only 4 trials and concluded that self-management education has some evidence of benefit but did not find clear evidence of substantially improved outcomes for adults with epilepsy.

The current review was requested by the VA National Neurology Program Office in the Office of Specialty Care Services, which is responsible for policies and programs for neurological disorders in the VHA nationally. The review will be used to identify the current evidence base and its quality to support the use of self-management programs aimed at patients with epilepsy, and identify potential barriers in the adoption of these programs within the VHA system. Prior systematic reviews on this topic were inadequate for the needs of our stakeholders because they did not include recent important studies; did not adequately consider components such as peer support, which has particular relevance to Veterans; and did not address implementation of self-management interventions.

# METHODS

We followed a standard protocol for this review. Each step was pilot-tested to train and calibrate study investigators. The PROSPERO registration number is CRD42018098604. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines.[25]

## TOPIC DEVELOPMENT

This topic was nominated by the VA National Neurology Program Office in the Office of Specialty Care Services, which is responsible for policies and programs for neurological disorders in the VHA nationally. The review will be used to identify the current evidence base and its quality to support the use of self-management programs aimed at patients with epilepsy, and identify potential barriers in the adoption of these programs within the VHA system.

### Key Questions

The Key Questions (KQs) for this report were:

**KQ 1:** For adults with epilepsy, what are the most commonly employed components of self-management interventions evaluated in comparative studies?

**KQ 2:** What are the effects of self-management interventions on self-management skills and self-efficacy, clinical outcomes, and health care utilization?

**KQ 3:** What are the identified facilitators and barriers that impact the adoption of self-management interventions in large-scale health systems such as the VHA?

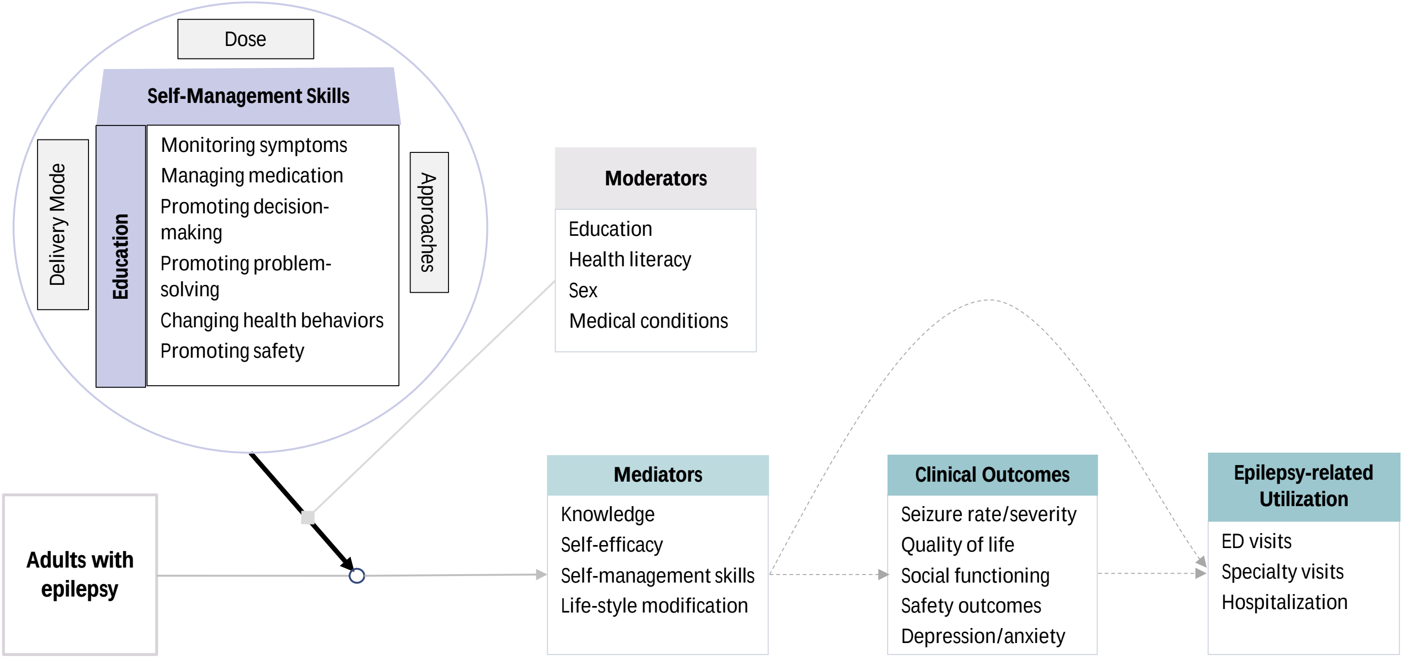
### Conceptual Framework

Most clinical outcomes for chronic conditions are mediated by daily patient-initiated behaviors outside of the health care setting,[26] underscoring the importance of developing effective self-management strategies. Following a review of self-management definitions, Jonkman and colleagues constructed an exact but flexible operational definition for self-management to maximize external validity without being overly restrictive.[27] We adopted their operational definition for the current review with 2 modifications. To increase the breadth of eligible interventions, we required only 1 component beyond knowledge acquisition (instead of 2 components). We also specified that decision-making skills should be for epilepsy-relevant behaviors such as epilepsy treatment management, safety promotion (*eg*, driving,), and changing relevant health behaviors (including stress management, sleep, and substance use). Our modified operational definition follows:

> Self-management interventions aim to equip patients with skills to actively participate and take responsibility in the management of their epilepsy in order to function optimally through knowledge acquisition and a combination of at least 1 of the following behaviors: stimulation of independent sign/symptom monitoring, medication management, enhancing problem-solving and decision-making skills for medical treatment management, safety promotion, and changing physical activity, dietary, and/or smoking behavior.

The conceptual model (Figure 1) outlines the population, intervention, outcomes, and potential effect moderators. The self-management interventions map to our modified definition but also include important contextual elements such as the delivery mode (*eg*, in-person, group, web-based), dose (*eg*, duration and frequency of contacts), and specific approaches used (*eg*, cognitive behavioral therapy). Potential effect moderators were identified based on patient characteristics that may be associated with different intervention effects.

**Figure 1. Conceptual Model for Self-management of Epilepsy**



## SEARCH STRATEGY

In collaboration with an expert reference librarian, we conducted a primary search from inception through April 13, 2018, of MEDLINE® (via PubMed®), Cochrane Central Register of Controlled Trials (CENTRAL), PsycINFO, and CINAHL. We updated the MEDLINE search on October 31, 2018. We used a combination of MeSH keywords and selected free-text terms (*eg*, epilepsy, self-management, self-care) to search titles and abstracts (Appendix A). We also conducted hand-searches of references from selected high-quality systematic reviews and exemplar studies identified during the topic development process and as identified by our stakeholders.

Our search strategy was informed by the Cochrane Effective Practice and Organization of Care (EPOC) Group.[28] EPOC criteria were developed to capture both randomized and nonrandomized study designs. All citations were imported into 2 electronic databases (for referencing, EndNote®, Clarivate Analytics, Philadelphia, PA; for data abstraction, DistillerSR; Evidence Partners Inc., Manotick, ON, Canada).

## STUDY SELECTION

We used artificial intelligence (AI) technology developed as part of the DistillerSR software program (DistillerAI; Evidence Partners Inc., Manotick, ON, Canada) to assist with screening abstracts. Using prespecified inclusion/exclusion criteria (Table 1), the titles and abstracts of a subset of articles, enriched for potential relevance to the study questions (approximately 100) identified through our primary search and prior reviews, were classified independently by 2 senior investigators for relevance to the KQs. After resolving disagreements between the investigators, this set of included and excluded articles was used to train DistillerAI.[29]

DistillerAI was used to screen the remaining titles and abstracts using a "high confidence" approach that employs 2 algorithms to classify citations. All citations classified by DistillerAI with certainty (*ie*, eligible or ineligible) underwent abstract review by 1 investigator. All other citations (50%) underwent abstract screening by 2 investigators. Articles included by an investigator or AI algorithm underwent full-text screening by 2 investigators. Disagreements were resolved by consensus between the investigators or by a third investigator. Articles meeting all eligibility criteria were included for data abstraction.

**Table 1. Eligibility Criteria**

| Study Characteristic | Include | Exclude |
|---|---|---|
| **Population** | · Adults (aged ≥18) with new or chronic epilepsy<br>· Family members and/or caregivers of those with epilepsy<br>· KQ 3 only: Stakeholders involved in implementation (*eg*, neurologists, health coaches, nurses, administrators) | · Children<br>· Populations with <70% adults<br>· Severe learning disabilities<br>· Non-epileptic seizures (*ie*, psychogenic seizures)<br>· Populations who have been recruited for depression or who have major mental illness (*eg*, bipolar, major depressive disorder, schizophrenia) |
| **Intervention** | Self-management defined as interventions that aim to equip patients with skills to actively participate and take responsibility in the management of epilepsy in order to function optimally through at least knowledge acquisition and a combination of 1 or more of the following:<br>· Stimulation of independent sign/symptom monitoring<br>· Medication management<br>· Enhancing problem-solving and decision-making skills for epilepsy treatment management, safety promotion (*eg*, driving)<br>· Changing health behaviors (including stress management, sleep, substance use)[a] | ● Multicomponent interventions that include self-management but where self-management is not the primary intervention<br>● Cognitive behavioral therapy focused on comorbid mental illness in patients with epilepsy (*eg*, depression in patients with epilepsy)<br>● Education-only interventions<br>● General care delivery interventions (*eg*, introducing specialist nurse practitioner or implementation of clinical practice guidelines) |

| Study Characteristic | Include | Exclude |
|---|---|---|
| | Examples include:<br>- Psychoeducation (*eg*, cognitive behavioral therapy)<br>- Behavioral interventions (*eg*, adherence strategy training)<br>- Personalized care plan development and coaching | |
| **Comparator** | Any (usual care, attention control, active intervention) | None |
| **Outcomes** | Self-management skills/self-efficacy<br>- Epilepsy self-efficacy and epilepsy self-management scales[b]<br>- Medication adherence[b]<br>- Disease knowledge<br>Clinical<br>- Seizure rate/frequency/severity[b]<br>- Quality of life[b]<br>- Social function/engagement (*eg*, days work missed, or validated measure)[b]<br>- Psychological symptoms (*ie*, distress, depressive or anxiety symptoms)<br>- Safety outcomes (*eg*, motor vehicle accidents)[b]<br>- Medication toxicity<br>Health care utilization<br>Acute care or emergency department visits, hospitalization, or outpatient specialty visits for epilepsy | None |
| **Timing** | KQ 1, KQ 2:<br>- Must be longitudinal (any length)<br>- Assessments at end of treatment and longest follow-up | KQ 1, KQ 2:<br>Cross-sectional or assessments at the time of intervention delivery |
| **Setting** | - Delivered in person (individual or group) in outpatient settings, or remotely via telehealth technology (*eg*, mobile or internet)<br>- Delivered by health care team members or trained layworkers | - Inpatient<br>- Delivered only in emergency departments |
| **Design[b]** | KQ 1, KQ 2:<br>- Randomized trials<br>- Nonrandomized trials<br>- Controlled before-after studies[c]<br>- Prospective cohort study if it includes a properly adjusted analysis | KQ 1, KQ 2:<br>- Self-described pilot studies and/or sample size <20<br>- Studies with retrospective data collection<br>- Interrupted time series<br>- Case series |

| Study Characteristic | Include | Exclude |
|---|---|---|
| | KQ 3:<br>- Above KQ study designs<br>- Qualitative and survey designs if specifically addressing facilitators and barriers to adoption of epilepsy self-management interventions | - Systematic reviews/meta-analyses<br>KQ 3:<br>· Reports that do not include primary data on barriers or facilitators |
| **Language** | English | Non-English |
| **Countries** | OECD[d] | Non-OECD |
| **Years** | Any | None |
| **Publication Types** | Full publication in a peer-reviewed journal | Letters, editorials, reviews, dissertations, meeting abstracts, protocols without results |

[a] Adapted from Jonkman et al, 2016.27

[b] Outcomes prioritized for synthesis. For other outcomes, only the frequency of reporting is described.

[c] See Cochrane EPOC criteria for definitions and details.28

[d] OECD = Organization for Economic Cooperation and Development includes Australia, Austria, Belgium, Canada, Chile, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Korea, Latvia, Luxembourg, Mexico, Netherlands, New Zealand, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom, United States.

Abbreviation: KQ=Key Question

## DATA ABSTRACTION

Data from published reports were abstracted into a customized DistillerSR database by 1 reviewer and over-read by a second reviewer. Disagreements were resolved by consensus or by obtaining a third reviewer's opinion when consensus was not reached. Data elements included descriptors to assess applicability, quality elements, intervention/exposure details, and outcomes.

Key characteristics abstracted were patient descriptors (*eg*, age, sex, race, duration of epilepsy if available), intervention characteristics (*eg*, interventionist if targeting family member/caregiver, delivery modality, duration/intensity, key intervention components, peer support), comparator, and outcomes, as described previously. For studies relevant to KQ 3, we abstracted barriers (*ie*, description of themes or factors that impeded the use and implementation of the intervention as reported in the study's results and/or findings sections) and facilitators (*ie*, description of themes or factors that aided the use of the intervention as reported in the study's results and/or findings sections) to the implementation of self-management interventions (as distinct from barriers and facilitators of an individual engaging in self-management behaviors). In addition, we abstracted respondent characteristics (*eg*, if respondent was a patient with epilepsy, caregiver, or health care provider), and design details (*eg*, semi-structured interviews, cross-sectional surveys, open-ended questions). Multiple reports from a single study were treated as a single data point, prioritizing results based on the most complete and appropriately analyzed data. When critical data were missing or unclear in published reports, we requested supplemental data from the study authors. Key features relevant to applicability included the match between the sample and target populations (*eg*, age, Veteran status).

## QUALITY ASSESSMENT

Quality assessment was done by the investigator abstracting or evaluating the included article and was over-read by a second, highly experienced investigator. Disagreements were resolved by consensus between the 2 investigators or, when needed, by arbitration by a third investigator.

For KQ 1 and KQ 2, we used the Cochrane EPOC risk of bias (ROB) tool, which is applicable to randomized and nonrandomized studies.[28] These criteria are adequacy of randomization and allocation concealment; comparability of groups at baseline; blinding; completeness of follow-up and differential loss to follow-up; whether incomplete data were addressed appropriately; validity of outcome measures; protection against contamination; selective outcomes reporting; and conflict of interest. We assigned a summary ROB score (low, unclear, high) to individual studies separately for non–patient reported outcomes, hereafter referred to as objective outcomes (*eg,* emergency department visits), and patient-reported outcomes (*eg*, quality of life).

Summary ROB ratings are defined as follows:

- Low ROB: Bias, if present, is unlikely to alter the results seriously.
- Unclear ROB: A risk of bias that raises some doubts about the results.
- High ROB: Bias may alter the results seriously.

For KQ 3 qualitative studies, we utilized 3 ROB forms for different study designs. For qualitative studies (n=5), we adapted the 10-item Critical Appraisal Skills Programme (CASP) for Qualitative Research Studies.[30] Each item is rated “Yes,” “No,” or “Can’t tell”; there is no summary rating. For the remaining studies, we adapted the Mixed Methods Appraisal Tool (MMAT).[31] For the quantitative descriptive studies (n=7) we used the 5-item MMAT specific to quantitative descriptive studies. These criteria address the sampling strategy, the sample representativeness, measurements, risk of nonresponse bias, and appropriateness of the statistical analysis. For the mixed methods study (n=1), we used the 5-item MMAT specific to mixed methods studies. These criteria address the rationale for using mixed methods, the integration of the study components, the interpretation of the study components, discussion of divergences or inconsistencies between the quantitative and qualitative data, and how each component of the study adheres to the quality criteria of each of the quantitative and qualitative methods. The MMAT rates each item “Yes,” “No,” or “Can’t tell”; there is no summary rating. Details on quality assessment criteria are presented in the Glossary.

## DATA SYNTHESIS

We summarized the primary literature using relevant data abstracted from the eligible studies. Summary tables describe the key study characteristics of the primary studies: study design, patient demographics, and details of the intervention and comparator. We initially planned to classify studies into those meeting the full definition of self-management[27] and those with fewer components. However, studies were classified more naturally into 2 categories, those emphasizing education and those emphasizing skill acquisition from psychosocial therapy approaches.

We then determined the feasibility of completing a quantitative synthesis (*ie*, meta-analysis) to estimate summary effects (KQ 2). For meta-analyses, feasibility depends on the volume of relevant literature, conceptual homogeneity of the studies, and completeness of results reporting. We aggregated outcomes when there were at least 3 studies with the same outcome, based on the rationale that 1 or 2 studies do not provide adequate evidence for summary effects. When quantitative synthesis was feasible, we stratified by study design (randomized vs nonrandomized) and by intervention category. Although we planned to evaluate the consistency of effects by components of the intervention, there were too few studies to perform these analyses.

When quantitative synthesis was possible, outcomes were summarized using the mean difference (MD) when all studies reported the outcome using the same scale (*eg*, quality of life), and standardized mean difference (SMD) for outcomes using different measures for the same construct (*eg*, medication adherence). The SMD is the difference in outcomes between the intervention and comparator, divided by the pooled standard deviation. Cohen suggested the following guidelines for interpreting the magnitude of the SMD: small = 0.2; medium = 0.5; and large = 0.8.[32] For analyses with few (n <20) studies, we used the Knapp-Hartung approach[33] to adjust the standard errors of the estimated coefficients. When intervention effects varied importantly across studies, we conducted a sensitivity analyses to omit studies judged to be at high risk of bias. We evaluated for statistical heterogeneity using visual inspection and Cochran's Q and $I^2$ statistics. Test statistics for publication bias (*eg*, Begg's or Egger's regression statistics) only perform adequately when there are more than 10 studies in an analysis. Since no analyses met this threshold, formal analyses for publication bias were not performed.

When quantitative synthesis was not feasible, we analyzed the data narratively. We gave more weight to the evidence from higher-quality studies with more precise estimates of effect. Qualitative synthesis focused on documenting and identifying patterns in efficacy and safety of the interventions across conditions and outcome categories. We analyzed potential reasons for inconsistency in treatment effects across studies by evaluating differences in the study population, intervention, comparator, and outcome definitions.

For the KQ 3 analysis, we created a qualitative team composed of 2 co-investigators (AAL, AS) who had experience in qualitative methodology. Under the guidance of the primary investigator (JWW), the qualitative co-investigators led the abstraction and analysis of data collected for KQ 3. We analyzed the abstracted data from the KQ 3 studies using thematic synthesis and the framework method.[34,35] Using the KQ 3 question as a guide, we created an *a priori* framework based on the ecological framework[36] that included barriers and facilitators as reported for a category (*eg*, patient with epilepsy or caregiver; program or intervention; and site or health system). All abstracted findings were categorized; data could be in only 1 framework (*eg*, a facilitator or a barrier) and in only 1 category (*eg*, patient/caregiver, program/intervention, site/health system). We then completed first-level analysis of these data and confirmed the validity of our interpretations by referencing the original texts. After the data were independently coded and discussed among the 2 qualitative researchers, we conducted thematic synthesis by identifying and grouping related codes within each category (*eg*, patient/caregiver, program/intervention, site/health system). Then, each researcher independently organized related codes into themes. We reviewed the theme development and then identified overarching themes that applied to both facilitators and barriers. The creation and identification of codes and themes was iterative; to ensure rigor and validity of these findings, we independently coded and developed themes and then discussed theme development and identification until we reached agreement between the 2 researchers.

## RATING THE BODY OF EVIDENCE

The certainty of evidence (COE) for each KQ was assessed using the approach described by Grading of Recommendations Assessment, Development and Evaluation (GRADE).[37] We limited GRADE ratings to those outcomes identified by the stakeholder and Technical Expert Panel (TEP) as critical to decision-making. In brief, this approach requires assessment of 4 domains: risk of bias (ROB), consistency, directness, and precision. Additional domains to be used when appropriate are coherence, dose-response association, impact of plausible residual confounders, strength of association (magnitude of effect), and publication bias. These domains were considered qualitatively, and a summary rating was assigned after discussion by 2 investigators as high, moderate, or low strength of evidence. In some cases, high, moderate, or low ratings were impossible or imprudent to make. In these situations, a grade of insufficient was assigned.

## PEER REVIEW

A draft version of this report was reviewed by technical experts and clinical leadership. A transcript of their comments and our responses is in Appendix B.

# RESULTS

## ORGANIZATION OF THE RESULTS

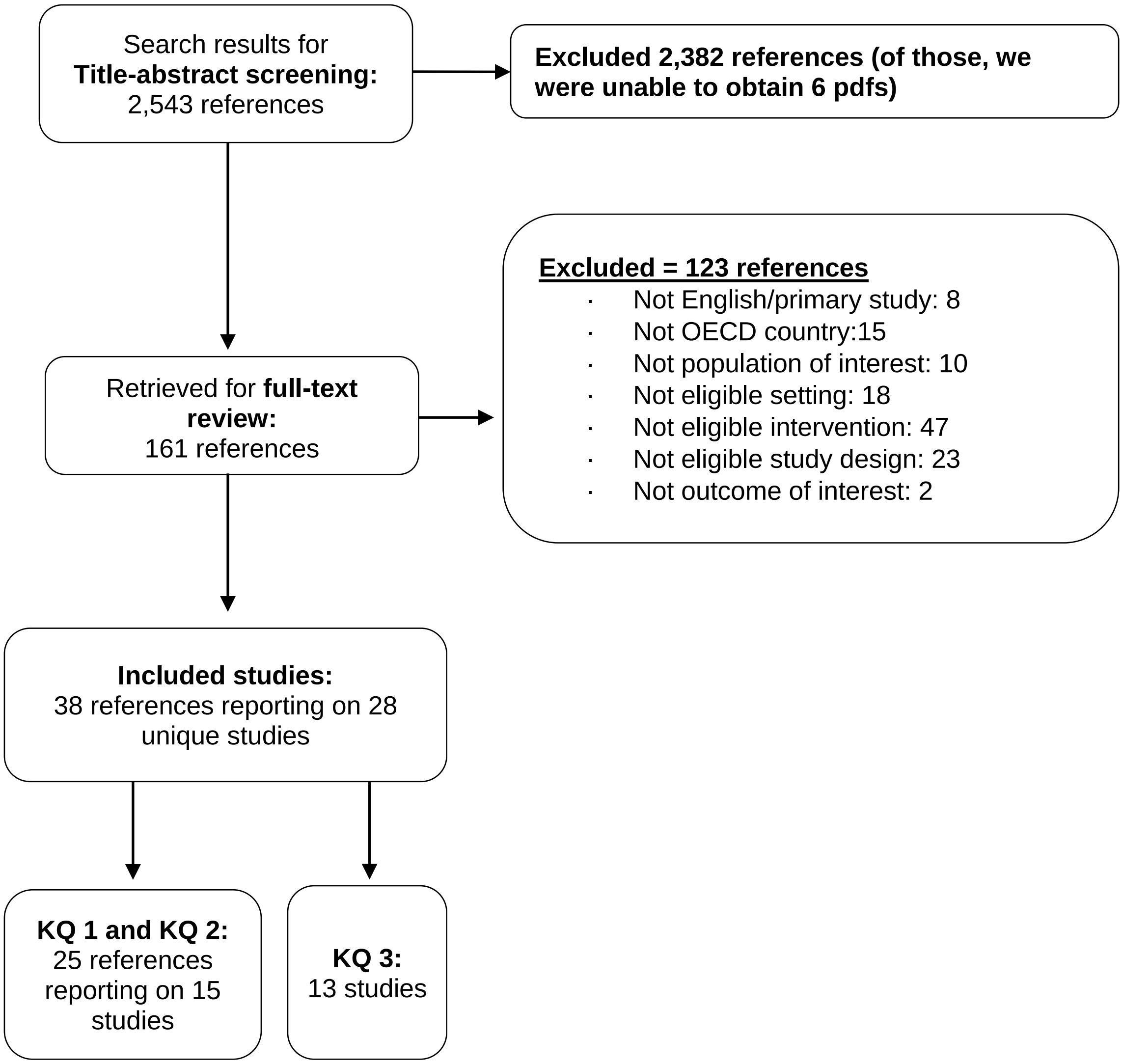
The results are organized to first report the yield of the literature search and the pattern of reported outcomes. Results are then reported for each KQ. For KQ 2, intervention effects are reported by category (*eg*, educational and psychosocial self-management interventions) and within the categories by primary and secondary outcomes.

## LITERATURE FLOW

We identified 2,535 studies through searches of MEDLINE® (via PubMed®), Cochrane Central Register of Controlled Trials (CENTRAL), PsycINFO, and CINAHL (Figure 2). An additional 8 articles were identified through reviewing bibliographies of relevant review articles,[38-45] for a total of 2,543 articles. After applying inclusion and exclusion criteria to titles and abstracts, 161 articles remained. Fifteen unique studies relevant to KQs 1 and 2 were retained for data abstraction, of which 13 were randomized and 2 were nonrandomized. Thirteen studies relevant to KQ 3 were retained for data abstraction. All studies were conducted in the United States, Canada, Europe, or Australia.

Appendix C presents detailed intervention characteristics, and Appendix D contains detailed study characteristics. Appendix E lists the excluded studies and reasons for exclusion. Appendix F contains a glossary of terms.

## Figure 2. Literature Flow Chart

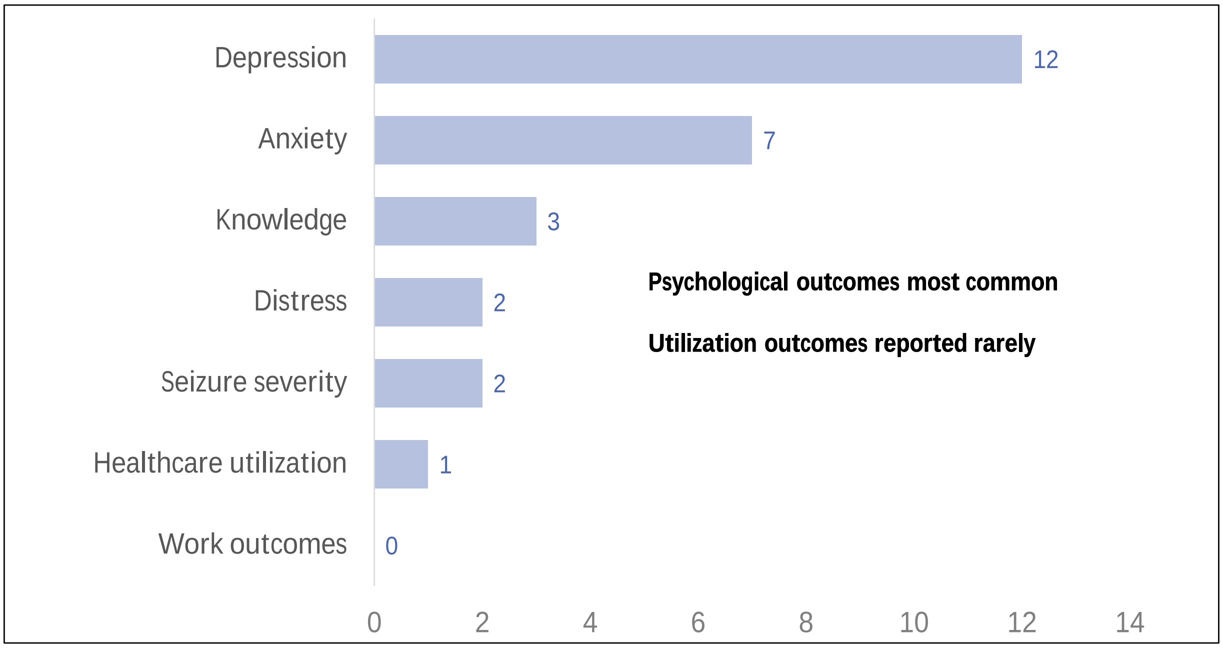


## PATTERNS OF OUTCOME REPORTING

With input from the TEP, outcomes were grouped into those for synthesis (primary, secondary outcomes) and those for which the frequency of reporting would be described. The primary and secondary outcomes are described in detail in KQ 2.

The pattern of outcomes identified for description but not synthesis is shown in Figure 3. Effects on psychological symptoms were reported frequently. Effects on health care utilization and work outcomes (*eg*, employment, productivity) were not reported.

**Figure 3. Pattern of Outcome Reporting (15 Studies)**



**Psychological outcomes most common**

**Utilization outcomes reported rarely**

## KEY QUESTION 1: For adults with epilepsy, what are the most commonly employed components of self-management interventions evaluated in comparative studies?

### Key Points

- Self-management interventions used 2 approaches:
    - Educational interventions with content *created* specifically for patients with epilepsy (7 studies/interventions).
    - Psychosocial therapy interventions (*eg*, cognitive behavioral therapy [CBT], problem solving therapy [PST], progressive muscle relaxation [PMR]) established for other conditions and *adapted* for patients with epilepsy (8 studies/11 interventions).
- Both intervention approaches used a median of 4 self-management components:
    - All addressed education, implicitly or explicitly.

  - Most also addressed these components: stimulation of independent sign/symptom monitoring; enhancing problem-solving and decision-making skills for medical treatment management; and changing physical activity, dietary, and/or smoking behaviors.

- Studies delivered 4-16 hours of educational training. One study used self-paced internet-delivered modules, but most studies delivered the intervention face-to-face. Caregivers or family members were included in a minority of studies.
- Within educational interventions, 1 study explicitly provided a web-based forum for peer support, and 3 studies included peers as group leaders. Of the psychosocial therapy interventions, 3 utilized group sessions but did not clearly describe the facilitation of peer support, although it potentially could have occurred.
- Goal-setting with patients was present in only 3 educational interventions but present in 6 psychosocial therapy interventions across 5 studies.

## Detailed Findings

We identified 15 studies that met our inclusion criteria[46-60] and mapped them to the 6 components described in the operational definition: (1) knowledge acquisition, (2) stimulation of independent sign/symptom monitoring, (3) medication management, (4) enhancing problem-solving and decision-making skills for medical treatment management, (5) safety promotion, and (6) changing physical activity, dietary, and/or smoking behaviors. Because some studies had more than 1 active intervention arm, a total of 18 intervention arms are described across the 15 studies. There was a median of 4 self-management components per intervention arm (range 2-6; Table 2). Medication management and safety promotion were the least frequently addressed components. (Refer to Appendix C for detailed intervention characteristics and Appendix D for study characteristics.)

**Table 2. Components Across the 15 Studies (18 Intervention Arms)**

| Study Acronym Design | Knowledge | Symptom Monitoring | Medication Management | Problem-solving | Safety | Health Behaviors | Total Components |
|---|---|---|---|---|---|---|---|
| *Educational Self-management Interventions* | | | | | | | |
| DiIorio, 2011[47]<br>WebEase<br>Randomized | Y | Y | Y | Y | N | Y | 5 |
| Fraser, 2015[48]<br>PACES<br>Randomized | Y | N | Y | Y | N | Y | 4 |
| Helgeson,1990[51]<br>SEE<br>Randomized | Y | N | Y | Y | N | N | 3 |
| May, 2002[53]<br>MOSES<br>Randomized | Y | Y | Y | Y | N | N | 4 |
| Ridsdale, 2018[57] | Y | Y | N | Y | Y | Y | 5 |

| Study<br>Acronym<br>Design | Knowledge | Symptom Monitoring | Medication Management | Problem-solving | Safety | Health Behaviors | Total Components |
|---|---|---|---|---|---|---|---|
| SMILE-UK<br>Randomized | | | | | | | |
| Sajatovic, 2018[58]<br>SMART<br>Randomized | Y | N | Y | Y | N | Y | 4 |
| Gunter, 2004[60]<br>Nonrandomized | Y | Y | N | N | N | N | 2 |
| *Psychosocial Therapy Self-management Interventions* | | | | | | | |
| Caller, 2016[46]<br>HOBSCOTCH<br>Randomized<br>Arm 1<br>Arm 2 | Y<br>Y | N<br>N | N<br>N | Y<br>Y | N<br>N | Y<br>Y | 3<br>3 |
| Gandy, 2014[49]<br>Randomized | Y | Y | Y | Y | N | Y | 5 |
| Haut, 2018[50]<br>Randomized | Y | Y | N | N | N | Y | 3 |
| Leenen, 2018[52]<br>ZMILE<br>Randomized | Y | Y | Y | Y | Y | Y | 6 |
| McLaughlin, 2011[54]<br>Randomized<br>Arm 1<br>Arm 2 | Y<br>Y | Y<br>Y | Y<br>N | Y<br>N | N<br>N | Y<br>Y | 5<br>3 |
| Puskarich, 1992[55]<br>Randomized | Y | N | N | N | N | Y | 2 |
| Tan, 1986[56]<br>Randomized | Y | Y | N | Y | N | Y | 4 |
| Gillham,1990[59]<br>Nonrandomized<br>Arm 1<br>Arms 2 & 3[a] | Y<br>Y | Y<br>Y | N<br>N | Y<br>Y | N<br>N | Y<br>Y | 4<br>4 |
| **Total arms** | **18** | **12** | **8** | **14** | **2** | **15** | |

[a] Arms 2 and 3 were assigned the same intervention in the initial intervention period of this crossover study.

In examining the components of each self-management intervention, we identified 2 distinct groups of interventions classified by emergent criteria: intervention focus (educational vs psychosocial therapy) and intervention development (created vs adapted for patients with epilepsy). The first group evaluated interventions that were created for patients and distinguished by a primary focus on education (Figure 4). Seven studies described explicit educational components with the implicit understanding that education may lead to skill acquisition.[47,48,51,53,57,58,60] The second group focused on skill acquisition and evaluated interventions adapted for patients from previously existing therapies (Figure 4). Eight studies examining a total of 11 interventions described explicit skills acquisition components from therapeutic techniques; education components were described explicitly in some studies but in others were implicit.[46,49,50,52,54-56,59] Within each of these groups of interventions, however, there was also diversity of duration and/or intensity of the intervention, composition and training of the intervention delivery team, mode(s) of delivery for the intervention, target(s) of the intervention, and components of self-management addressed (Figure 5).

**Figure 4. Components Addressed in Self-management Interventions**

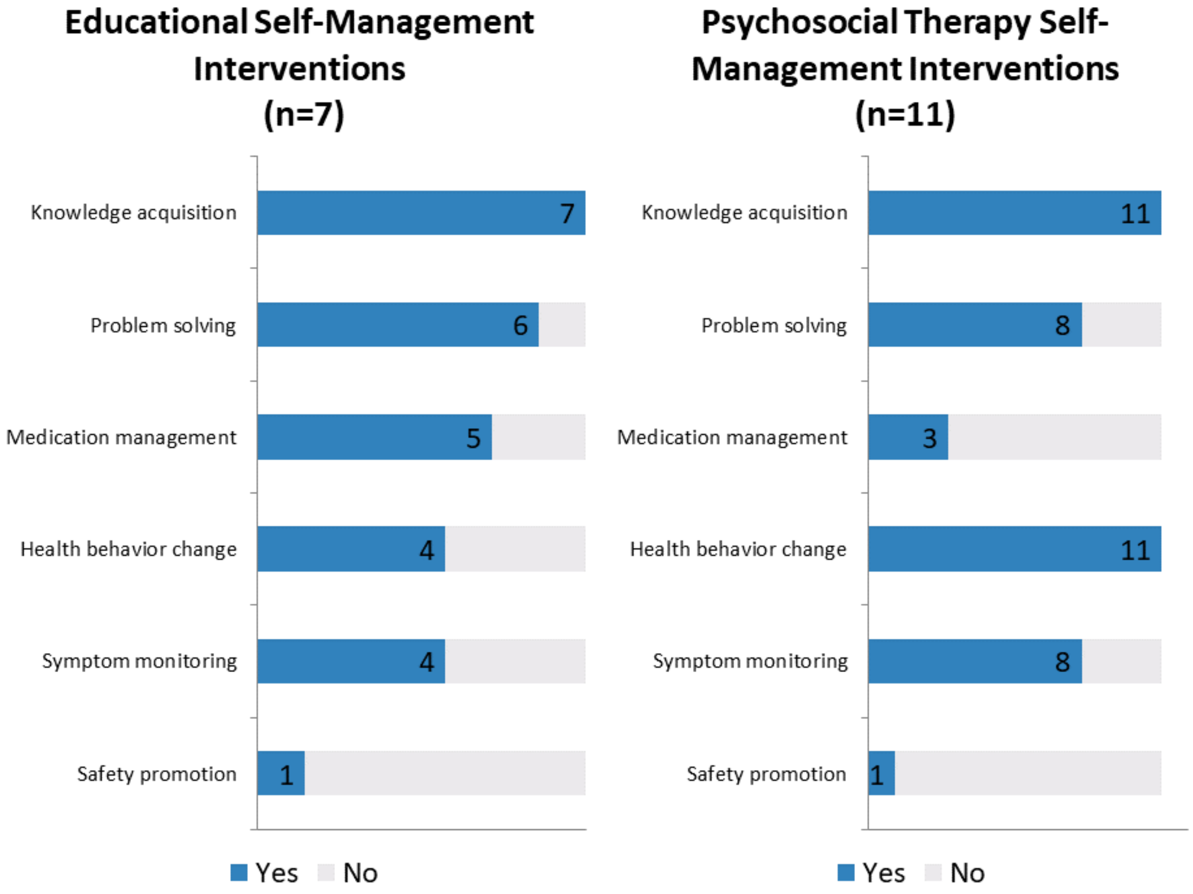
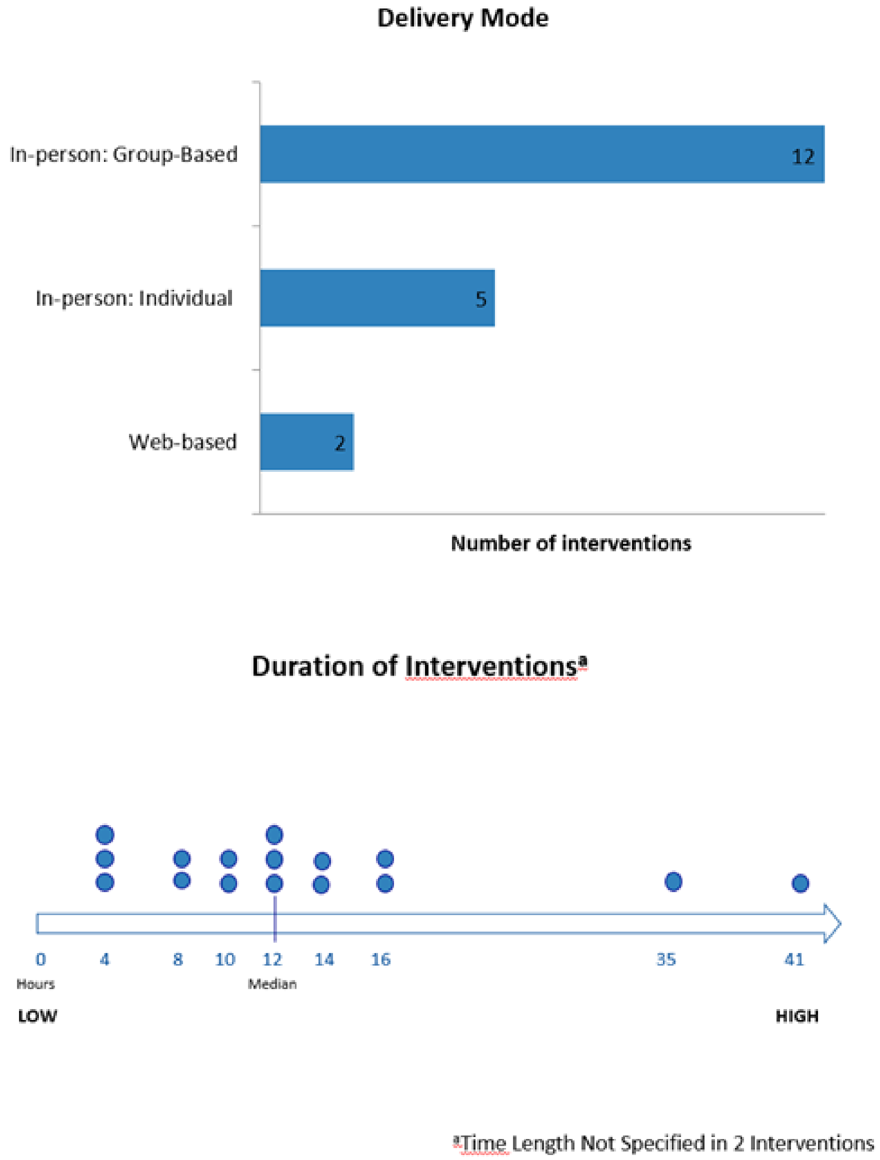


**Figure 5. Intervention Delivery Mode and Duration**



## Educational Self-management Interventions Created for Patients with Epilepsy

Techniques used in educational self-management interventions included presentation of modules and didactic discussions aimed at increasing knowledge around the symptoms, triggers, and psychological, social, and vocational problems that often arise with epilepsy. Modules also often addressed coping skills, problem-solving skills, self-monitoring skills, and medication management skills that can be helpful for patients. One study explicitly discussed safety concerns related to physical harm.[57] Five studies explicitly discussed symptom or seizure tracking, but only 2 had participants actively engage in this tracking through some form of diary or log. Only 3 studies incorporated some form of goal-setting with patients.[47,48,58]

Intervention duration varied considerably, with 2 interventions presenting durations that did not specify an amount of time because the intervention was a self-paced internet-delivered set of modules[47] or reported simply as 2 days of intervention for an unspecified number of hours.[51] The remaining intervention durations were generally 16 hours over 2 consecutive days, except for 2 interventions of 8 weekly sessions that varied from 60 to 90 minutes.[48,58] Interventions were primarily in-person, group-based didactic instruction and presentation; however, 1 study was delivered solely through asynchronous internet media,[47] 1 study began in-person and shifted to internet-based group didactic instruction and presentation, and 1 study was almost exclusively based on educational materials given to the patient within the context of a quality improvement intervention.[60] Intervention providers were not always specified but generally were either peers with epilepsy or a nurse practitioner, both with specific intervention training. Interventions were targeted to patients, but in 3 studies involving group intervention, caregivers and/or family members were allowed to attend sessions.[51,53,57] In addition to providing resources and education to patients, 1 intervention was developed to increase resources and education for practitioners providing care to patients.[60] Peer support was present in 3 studies, 2 of which involved trained peers as group facilitators,[48,53,58] and 1 of which involved discussions in online peer forums.[47]

### Psychosocial Therapy Self-management Interventions Adapted for Patients with Epilepsy

Techniques used in psychosocial therapy self-management interventions adapted for patients included broad multicomponent therapies, such as PST, CBT alone or paired with specific behavioral activation component or hierarchical stress inoculation, and “proactive coping skills” noted as being based on CBT principles. Some interventions used more specific techniques, such as PMR, cognitive training, and “brief psychological interventions” for problems like anxiety and depression. Six studies (7 interventions) evaluating psychosocial therapies also explicitly included some form of symptom or seizure monitoring.[49,50,52,54,56,59] Five studies explicitly discussed goal-setting with patients.[46,49,52,55,56]

Intervention duration varied between a total of 4 hours and 16 hours, with the majority of interventions comprising some form of weekly treatment with daily at-home practice of some skills. No intervention consisted of fewer than 4 independent contacts for treatment. Additionally, the most common mode of treatment was in-person group sessions but often included some form of asynchronous technological support (*eg*, seizure diary smartphone application or audiotape) to aid in independent practice of self-management. For 5 of the studies the delivery team comprised some form of nurse practitioner or psychologist (including psychological interns). One study noted a “therapist” delivered the intervention but did not specify further. The delivery team was not specified for 2 studies. The stated target for each of the interventions was patients with epilepsy. Two additional studies allowed caregivers and/or family members to attend sessions[52] or aid in identifying psychiatric/social issues for treatment.[59] Peer support features were not explicitly discussed in any intervention. However, 3 interventions involved group therapy, which could have facilitated peer support.[52,54,56]

## Summary of Findings

Overall, self-management interventions descriptively appeared to fall into 2 major categories: educational content created for patients with epilepsy or established psychosocial therapy interventions adapted for patients with epilepsy. Interventions had a median number of 4 self-management components, and this number did not differ between educational and psychosocial therapy intervention categories. The number of components ranged from 2 to 6. Interventions were generally of moderate intensity, ranging from 4 to 41 hours. However, the delivery of equally intense interventions varied; for example, 16 hours of intervention could have occurred in either 2 consecutive 8-hour days, or eight 2-hour sessions spread over 8 weeks. Peer support and family involvement were minimally present. Goal-setting with patients was frequently present in psychosocial therapy interventions, but infrequently present in educational interventions.

## KEY QUESTION 2: What are the effects of self-management interventions on self-management skills and self-efficacy, clinical outcomes, and health care utilization?

### Key Points

- Educational self-management interventions:
    - Primary outcomes: Interventions may improve the use of self-management practices, but the certainty of evidence (COE) is low; there was no effect on overall QOL (low COE) or seizure rates (moderate COE).
    - Secondary outcomes: There was no effect on self-efficacy, social function, or medication adherence.
- Psychosocial therapy self-management interventions:
    - Primary outcomes: Interventions had a positive effect on overall QOL (low COE) but no benefit on seizure rates (low COE); evidence was insufficient to determine effects on self-management practices.
    - Secondary outcomes: Sparse data suggest a possible benefit on self-efficacy; there were inconsistent effects on social function and limited data for no effect on medication adherence.
- One study of a group-based intervention in high-risk patients found no effect on the combined outcome of emergency department visits or hospitalizations. No studies reported effects on workplace productivity or employment status.
- Only 1 study reported enrolling Veterans.

### Detailed Findings

We identified 13 randomized[46-58] and 2 nonrandomized studies[59,60] (2,514 patients) that evaluated self-management interventions for patients with epilepsy. Most studies enrolled mid-life adults with at least some college education. Health literacy was not reported by any study. The median time since diagnosis of epilepsy was 18 years; focal epilepsy was the most common type. Over one-half of studies were conducted in the United States, and only one enrolled Veterans. Self-management was compared with usual care, waitlist, or attention controls in all but 1 randomized study, a study that compared 2 therapy interventions. The 2 nonrandomized studies utilized a crossover design to compare 2 therapy interventions,[59] and a cluster design to compare a quality improvement program with prominent educational features to usual care.[60] The risk of bias (ROB) for patient-reported outcomes was judged low for 3 studies,[50,52,57] unclear for 3 studies,[48,54,58] and high for 9 studies.[46,47,49,51,53,55,56,59,60] Table 3 shows the evidence profile for the studies. Detailed study characteristics are reported in Appendix D.

**Table 3. Evidence Profile for Studies of Self-management Interventions for Epilepsy (n=15)**

**Number of studies:** 13 randomized; 2 nonrandomized

**Study years:** 1986 to 2018

**Number of patients, total enrolled (range):** 2,514 (30-747)

**Women, median (range):** 63% (51-74)

**Race/ethnicity:** 72% white; not reported in 9 studies

**Age, median (range):** 41 (32-68)

**Education, median (range):** 52% any college or above (15-77); not reported in 6 studies

**Epilepsy duration, median (range):** 18 years (13-27); not reported in 4 studies

**Refractory epilepsy:** 3 studies

**Countries:** Australia, Austria, Canada, Germany, Netherlands, Switzerland, United Kingdom, United States

**Comparator:** Usual care, waitlist, or attention (13 studies); active (2 studies)

**Risk of bias, patient-reported outcomes:** 3 low, 3 unclear, 9 high

## Educational Self-management Interventions Created for Patients with Epilepsy

### *Primary Outcomes*

#### *Self-management*

Four randomized studies reported the effects of educational self-management interventions on self-management behaviors using the Coping With Epilepsy and Adaptation scale or the Epilepsy Self-Management Scale. Three studies provided sufficient information for meta-analysis.[48,53,58] These studies showed a moderate increase in self-management behaviors at 6-month follow-up (SMD 0.52; 95% CI 0.0 to 1.04; Figure 6). Intervention effects were consistent across studies (Q=2.8; p=0.24; $I^2$=29.8%). The fourth study documented a nonsignificant P value for improvement in self-management but did not offer further statistics and had a high ROB.[47] Overall, educational interventions created for patients with epilepsy suggest a possible benefit for self-reported measures of self-management and were judged at unclear or high ROB.

#### *Quality of Life*

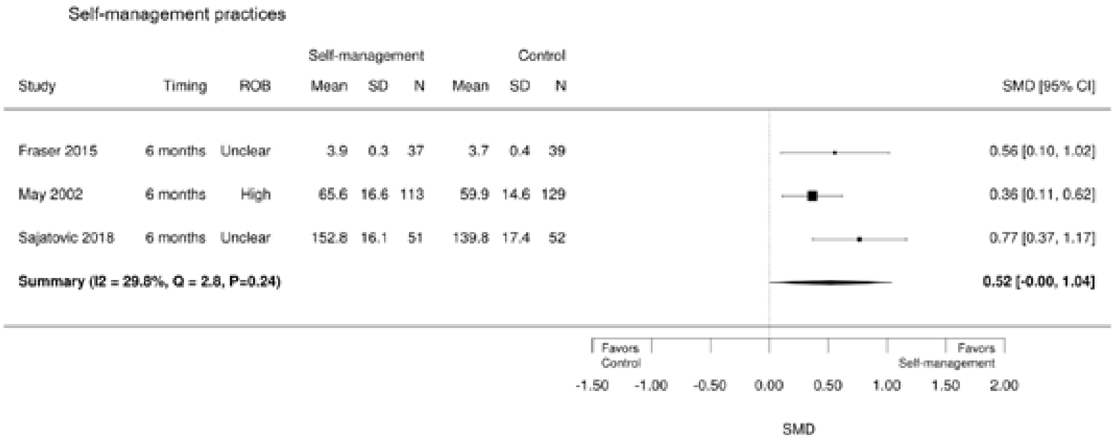
Four randomized studies and 1 nonrandomized study reported effects on QOL using the 10- or 31-item versions of Quality of Life in Epilepsy Inventory (QOLIE). The QOLIE overall score is calculated as a weighted average of 7 multi-item subscales and standardized to a 0-100 point total score; the minimum clinically important change has been reported as 11.8.[61] Three randomized studies provided sufficient data to summarize intervention effects (Figure 6). Overall, these 3 randomized studies showed no benefit on QOL (SMD 0.17; 95% CI -0.57 to 0.91), although there was heterogeneity in intervention effects across studies (Q=5.1; p=0.037;

$I^2$=60.8%). Both the larger low ROB study[57] and a small, unclear ROB study,[50] showed no intervention effect. A recent trial examining the novel SMART intervention showed a statistically significant improvement in quality of life over the 6 month study period (SMD 0.53; 95% CI 0.93 to 0.14),[58] a marked divergence from the other randomized education trials. A fourth large, high ROB study examined a web-based educational intervention and reported no effect on QOL (p=nonsignificant), but did not provide sufficient data to calculate an intervention effect.[47] An additional nonrandomized cluster study examined the effects of an educational intervention delivered within the context of a quality improvement study.[60] This large, high ROB study reported small improvements in QOL (£1.5 points) in the intervention and control arms that did not differ between groups (mean difference [MD] 0.5; 95% CI -6.4 to 7.4).

*Seizure Rates*

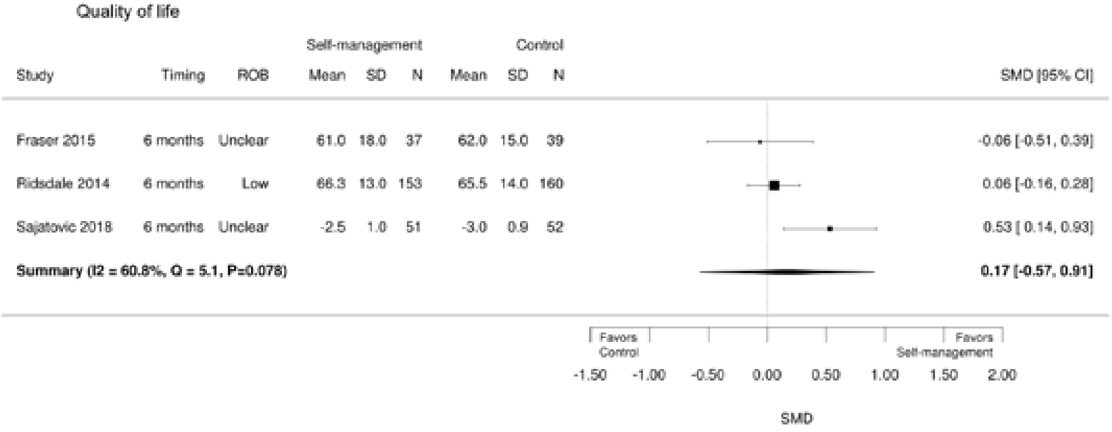
Four randomized studies reported intervention effects on self-reported seizure rates using multi-item scales, self-reported seizure count, a categorical measure, or an unspecified self-report method.[51,53,57,58] These studies, with mixed ROBs, demonstrated no impact of the group-based educational interventions on seizure frequency (SMD 0.0; 95% CI -0.03 to 0.04; Figure 6). Results were consistent across studies (Q=0.1; p=1.00; $I^2$=0.0%), and the confidence interval for the summary SMD excludes even a small clinically important effect.

## Figure 6. Effects of Educational Self-management Interventions on Primary Outcomes



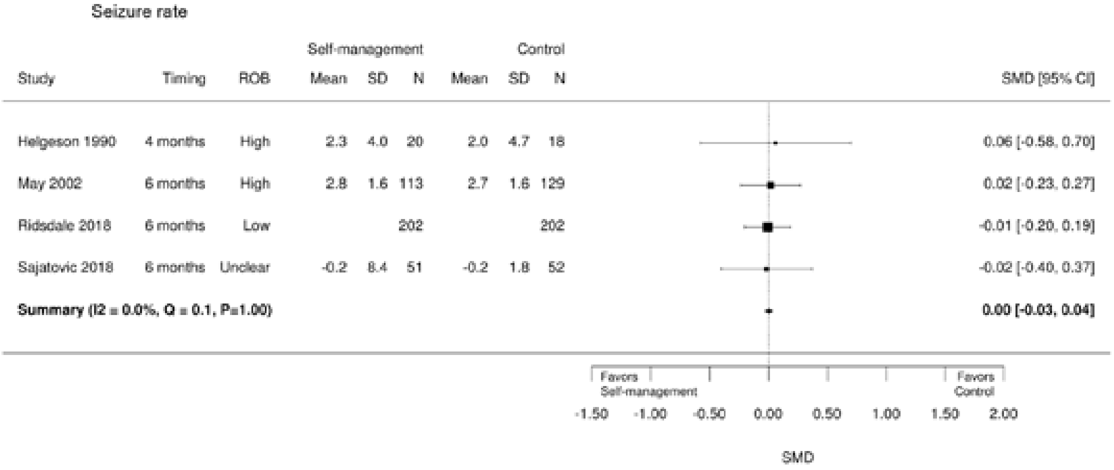
Self-management practices

| Study | Timing | ROB | Self-management Mean | Self-management SD | Self-management N | Control Mean | Control SD | Control N | SMD [95% CI] |
|---|---|---|---|---|---|---|---|---|---|
| Fraser 2015 | 6 months | Unclear | 3.9 | 0.3 | 37 | 3.7 | 0.4 | 39 | 0.56 [0.10, 1.02] |
| May 2002 | 6 months | High | 65.6 | 16.6 | 113 | 59.9 | 14.6 | 129 | 0.36 [0.11, 0.62] |
| Sajatovic 2018 | 6 months | Unclear | 152.8 | 16.1 | 51 | 139.8 | 17.4 | 52 | 0.77 [0.37, 1.17] |
| **Summary (I2 = 29.8%, Q = 2.8, P=0.24)** | | | | | | | | | **0.52 [-0.00, 1.04]** |



Quality of life

| Study | Timing | ROB | Self-management Mean | Self-management SD | Self-management N | Control Mean | Control SD | Control N | SMD [95% CI] |
|---|---|---|---|---|---|---|---|---|---|
| Fraser 2015 | 6 months | Unclear | 61.0 | 18.0 | 37 | 62.0 | 15.0 | 39 | -0.06 [-0.51, 0.39] |
| Ridsdale 2014 | 6 months | Low | 66.3 | 13.0 | 153 | 65.5 | 14.0 | 160 | 0.06 [-0.16, 0.28] |
| Sajatovic 2018 | 6 months | Unclear | -2.5 | 1.0 | 51 | -3.0 | 0.9 | 52 | 0.53 [ 0.14, 0.93] |
| **Summary (I2 = 60.8%, Q = 5.1, P=0.078)** | | | | | | | | | **0.17 [-0.57, 0.91]** |



Seizure rate

| Study | Timing | ROB | Self-management Mean | Self-management SD | Self-management N | Control Mean | Control SD | Control N | SMD [95% CI] |
|---|---|---|---|---|---|---|---|---|---|
| Helgeson 1990 | 4 months | High | 2.3 | 4.0 | 20 | 2.0 | 4.7 | 18 | 0.06 [-0.58, 0.70] |
| May 2002 | 6 months | High | 2.8 | 1.6 | 113 | 2.7 | 1.6 | 129 | 0.02 [-0.23, 0.27] |
| Ridsdale 2018 | 6 months | Low | | | 202 | | | 202 | -0.01 [-0.20, 0.19] |
| Sajatovic 2018 | 6 months | Unclear | -0.2 | 8.4 | 51 | -0.2 | 1.8 | 52 | -0.02 [-0.40, 0.37] |
| **Summary (I2 = 0.0%, Q = 0.1, P=1.00)** | | | | | | | | | **0.00 [-0.03, 0.04]** |

Abbreviations: CI=confidence interval; ROB=risk of bias; SD=standard deviation; SMD=standardized mean difference

Table 4 shows the COE for educational self-management interventions created for patients with epilepsy.

**Table 4. Certainty of Evidence for Educational Self-management Interventions Created for Patients with Epilepsy**

| Outcome | Number of Studies (Patients) | Findings | Certainty of Evidence (Rationale) |
|---|---|---|---|
| Epilepsy self-management | 4 randomized (569) | SMD 0.52 higher<br>(0 to 1.04 higher) | **Low certainty** of improved self-management<br>(rated down for serious ROB and reporting bias) |
| Quality of life | 4 randomized (492)<br>1 nonrandomized (747) | SMD 0.17<br>(0.57 lower to 0.91 higher)<br>MD 0.5<br>(6.4 lower to 7.4 higher) | **Low certainty** for no effect<br>(rated down for inconsistency and imprecision) |
| Seizure rates | 4 randomized (787) | SMD 0.00<br>(-0.3 lower to 0.04 higher) | **Moderate certainty** for no effect<br>(rated down for serious ROB) |

Abbreviations: MD=mean difference; NR=not reported; SMD=standardized mean difference; ROB=risk of bias

## *Secondary Outcomes*

### *Self-efficacy*

Four group-based educational self-management studies addressed self-efficacy at intervals between 2-12 months' follow-up.[48,51,57] Overall, interventions did not improve self-efficacy (SMD 0.18; 95% CI -0.32 to 0.69). However, intervention effects varied significantly (Q=8.0; p=0.045; $I^2$=62.7%). Studies varied importantly in timing of the outcome assessment (8 weeks to 12 months), which may be related to variable treatment effects. The one study showing moderate benefit delivered a stakeholder-informed, group-based intervention to patients (including veterans) at high risk for poor outcomes.[58] A fifth study (WebEase) that delivered the educational intervention online reported effects on self-efficacy as "p=NS" and could not be included in the meta-analysis.[47]

### *Social Function*

Effects of educational self-management interventions on social function were reported in 3 randomized studies[48,51,53] and 1 nonrandomized study.[60] Compared with controls, there were no effects of group-based self-management interventions on social function in randomized studies at 4-6 months follow-up (SMD -0.05; 95% CI -0.62 to 0.53; Figure 7). The nonrandomized study examined the effects of an educational intervention delivered within the context of a quality improvement study and reported no improvement on social function.

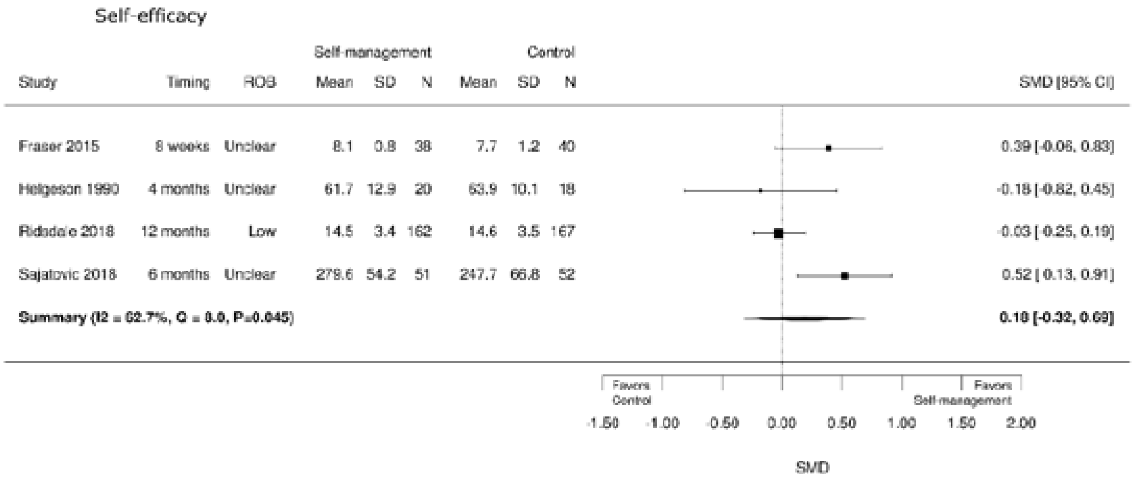
### *Medication Adherence*

Two educational self-management studies reported effects on medication adherence using self-report measures. Neither a web-based intervention (WebEase),[47] nor an in-person educational intervention (SMILE-UK)[57] improved medication adherence assessed at 6 weeks (SMD 0.05, 95% CI -0.32 to 0.43) and 12 months (SMD 0.0, 95%CI -0.22 to 0.22; Figure 7) respectively. A third randomized study, evaluated the Sepulveda Epilepsy Education program and inferred drug adherence based on antiepileptic drug levels at 4 months' follow-up.[51] Drug levels were significantly higher in the intervention group, but assessment of this outcome varied across treatment arms (85% vs 50%), which may have biased the results.

### *Emergency Department Visits and Safety*

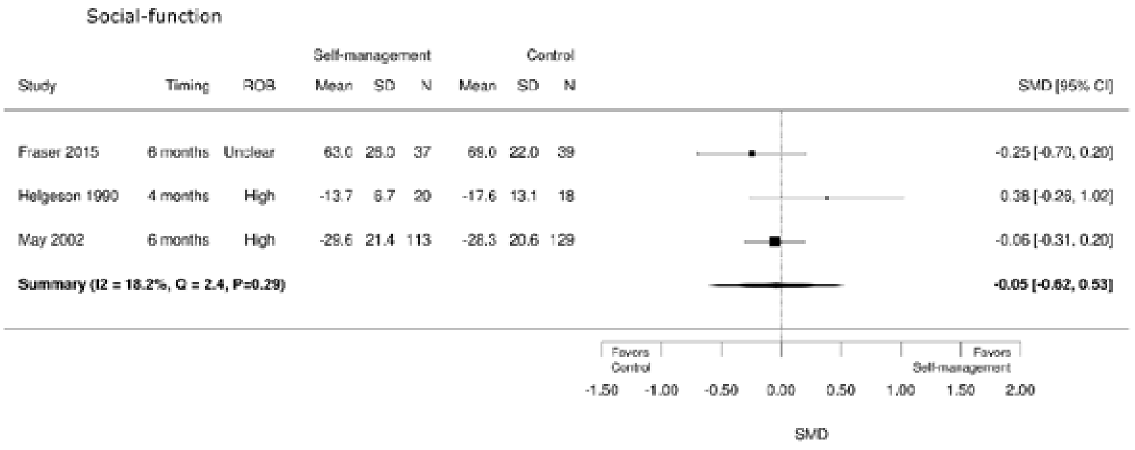
One education-based self-management study evaluated emergency department and hospital utilization.[58] The SMART intervention study reported 6-month changes in a composite measure of negative health events (seizures, emergency department visits, and hospitalizations) and emergency department visits or hospitalizations. Hospitalizations included all-cause admissions. Negative health events decreased more in the SMART education intervention group (mean change -10.16, SD 39.2) compared to waitlist control (mean change -1.93, SD 18.6; p = 0.04), but there was no significant improvement in emergency department and hospital utilization (p = 0.69).

## Figure 7. Effects of Educational Self-management Interventions on Secondary Outcomes



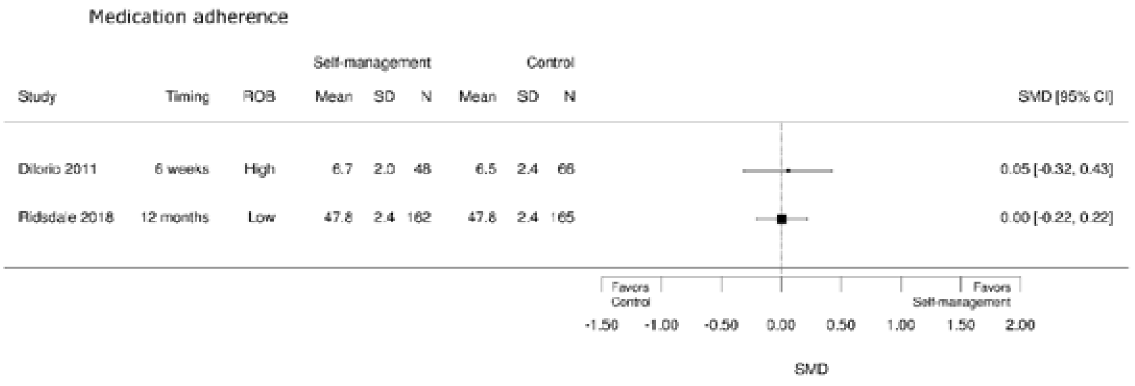
Self-efficacy

| Study | Timing | ROB | Self-management Mean | Self-management SD | Self-management N | Control Mean | Control SD | Control N | SMD [95% CI] |
|---|---|---|---|---|---|---|---|---|---|
| Fraser 2015 | 8 weeks | Unclear | 8.1 | 0.8 | 38 | 7.7 | 1.2 | 40 | 0.39 [-0.06, 0.83] |
| Helgeson 1990 | 4 months | Unclear | 61.7 | 12.9 | 20 | 63.9 | 10.1 | 18 | -0.18 [-0.82, 0.45] |
| Ridsdale 2018 | 12 months | Low | 14.5 | 3.4 | 162 | 14.6 | 3.5 | 167 | -0.03 [-0.25, 0.19] |
| Sajatovic 2018 | 6 months | Unclear | 279.6 | 54.2 | 51 | 247.7 | 66.8 | 52 | 0.52 [0.13, 0.91] |
| **Summary (I2 = 62.7%, Q = 8.0, P=0.045)** | | | | | | | | | **0.18 [-0.32, 0.69]** |



Social-function

| Study | Timing | ROB | Self-management Mean | Self-management SD | Self-management N | Control Mean | Control SD | Control N | SMD [95% CI] |
|---|---|---|---|---|---|---|---|---|---|
| Fraser 2015 | 6 months | Unclear | 63.0 | 26.0 | 37 | 68.0 | 22.0 | 39 | -0.25 [-0.70, 0.20] |
| Helgeson 1990 | 4 months | High | -13.7 | 6.7 | 20 | -17.6 | 13.1 | 18 | 0.38 [-0.26, 1.02] |
| May 2002 | 6 months | High | -29.6 | 21.4 | 113 | -28.3 | 20.6 | 129 | -0.06 [-0.31, 0.20] |
| **Summary (I2 = 18.2%, Q = 2.4, P=0.29)** | | | | | | | | | **-0.05 [-0.62, 0.53]** |



Medication adherence

| Study | Timing | ROB | Self-management Mean | Self-management SD | Self-management N | Control Mean | Control SD | Control N | SMD [95% CI] |
|---|---|---|---|---|---|---|---|---|---|
| DiIorio 2011 | 6 weeks | High | 6.7 | 2.0 | 48 | 6.5 | 2.4 | 66 | 0.05 [-0.32, 0.43] |
| Ridsdale 2018 | 12 months | Low | 47.8 | 2.4 | 162 | 47.8 | 2.4 | 165 | 0.00 [-0.22, 0.22] |

Abbreviations: CI=confidence interval; N=study sample size; ROB=risk of bias; SD=standard deviation; SMD=standardized mean difference

## Psychosocial Therapy Self-management Interventions Adapted for Patients with Epilepsy

### *Primary Outcomes*

#### *Self-management*

No studies of psychosocial therapy self-management interventions reported effects on self-management skills.

#### *Quality of Life*

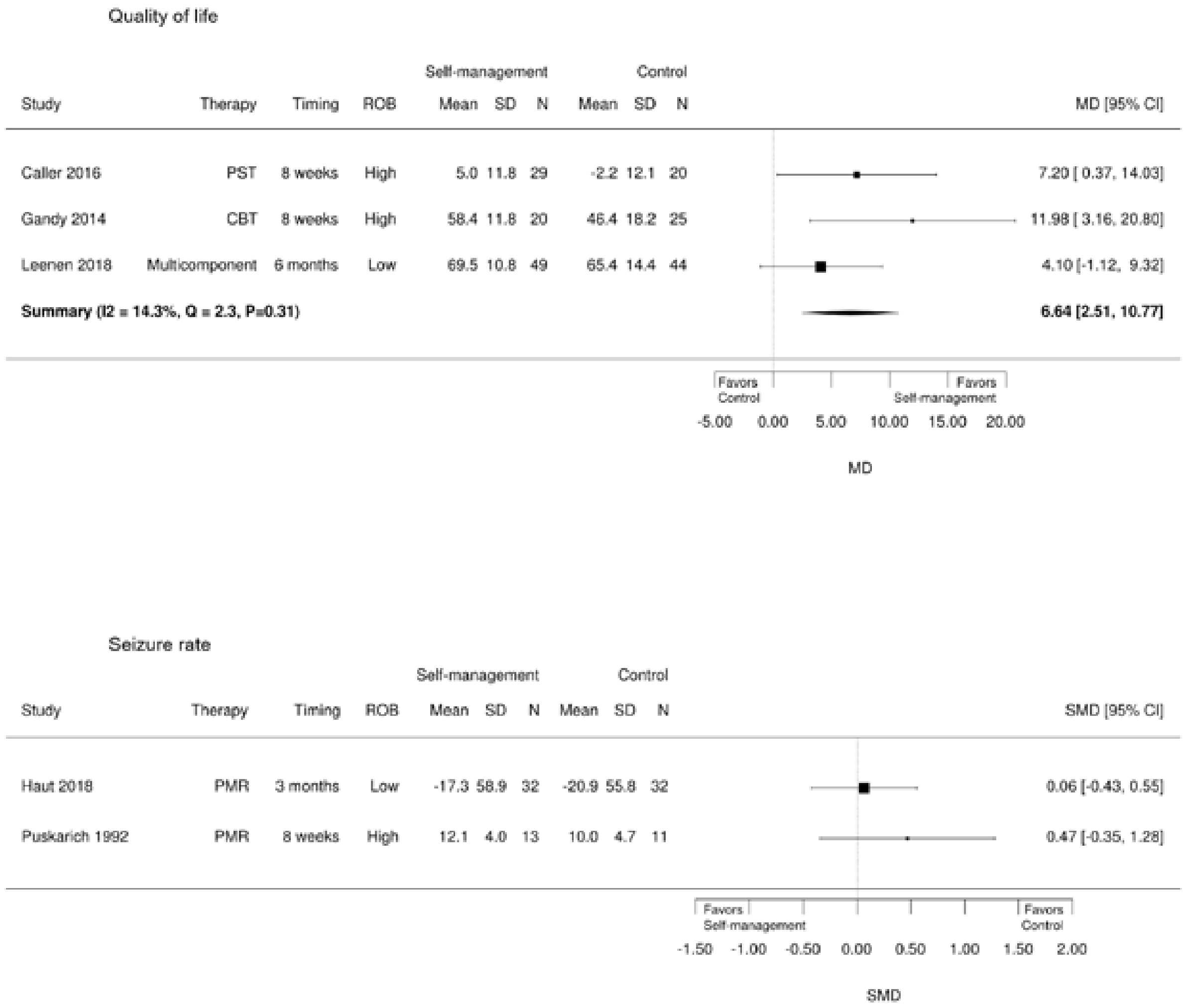
Three studies reported the effects of psychosocial therapy interventions on QOL; all measured QOL with the QOLIE. Studies evaluated problem-solving therapy with or without cognitive training,[46] CBT,[49] and a multicomponent self-management intervention (ZMILE) with an emphasis on self-management skills building and skill practice.[52] A larger, low ROB study showed small improvements in QOL at 3 and 6 months, but the confidence interval included no effect (MD 4.10; CI-1.12 to 9.32).[52] Two smaller, high ROB studies reported improvement in QOL. The first was an 8-week study with intensive (5 times per week) patient contact (MD 7.20; CI 0.37 to 14.03; Figure 8).[46] The second evaluated the effects of individual CBT on QOL at 2 and 3 months post-treatment and found a clinically important improvement in QOL at 3 months, though with a broad confidence interval (MD 11.98; CI 3.16 to 20.80, Figure 8).[49] The meta-analysis shows a likely positive effect for psychosocial therapy interventions on quality of life, but confidence intervals were broad and risk of bias was high.(MD 6.64; CI 2.51 to 10.77; Q=2.3; p=0.31; $I^2$=14.3%). A sensitivity analysis that adjusts the standard errors for small study effects resulted in a confidence interval that included no intervention effect (95% CI -2.45 to 15.73).

#### *Seizure Rates*

Three randomized studies and 1 nonrandomized study compared the effect of interventions to controls on seizure rates. The first, a small, low ROB study found no effect for progressive muscle relaxation compared to control at 3-month follow-up (SMD 0.06; 95%CI -0.43 to 0.55; Figure 8), though it did demonstrate a significant improvement from baseline rates.[50] A second small study also examined progressive relaxation training.[55] This high ROB study also demonstrated improvement in seizure rates from baseline for the intervention group, but no significant difference in average seizures when compared to control (SMD 0.47; 95% CI -0.35 to 1.28; Figure 8). Excluded from the forest plot because of insufficient data was a third small, high ROB trial that compared CBT with supportive counseling and waitlist control.[56] The study reported improvement with the therapy intervention (50% of patients in the CBT group failed to improve, vs 80%-89% of patients in the supportive counseling and control groups) that did not reach statistical significance. A single nonrandomized crossover study examining 2 psychosocial therapy interventions identified similar improvements in seizure rates from baseline to Week 42 regardless of the intervention or order of intervention.[59]

An additional small randomized study compared CBT with a relaxation therapy control.[54] We considered the relaxation arm an active intervention. The study, with unclear ROB, reported a significant improvement in seizure control in the CBT group versus relaxation control (Cohen's D 0.63; p <0.01), and further noted a time-dependent increase in the improvement in the CBT group over the 3-month follow-up period. Overall, these small studies evaluating psychosocial therapy self-management interventions did not show benefit on seizure rates when compared with control or another active intervention.

**Figure 8. Effects of Psychosocial Therapy Self-management Interventions on Primary Outcomes**



Quality of life

| Study | Therapy | Timing | ROB | Self-management Mean | Self-management SD | Self-management N | Control Mean | Control SD | Control N | MD [95% CI] |
|---|---|---|---|---|---|---|---|---|---|---|
| Caller 2016 | PST | 8 weeks | High | 5.0 | 11.8 | 29 | -2.2 | 12.1 | 20 | 7.20 [ 0.37, 14.03] |
| Gandy 2014 | CBT | 8 weeks | High | 58.4 | 11.8 | 20 | 46.4 | 18.2 | 25 | 11.98 [ 3.16, 20.80] |
| Leenen 2018 | Multicomponent | 6 months | Low | 69.5 | 10.8 | 49 | 65.4 | 14.4 | 44 | 4.10 [-1.12, 9.32] |
| **Summary (I2 = 14.3%, Q = 2.3, P=0.31)** | | | | | | | | | | **6.64 [2.51, 10.77]** |

Seizure rate

| Study | Therapy | Timing | ROB | Self-management Mean | Self-management SD | Self-management N | Control Mean | Control SD | Control N | SMD [95% CI] |
|---|---|---|---|---|---|---|---|---|---|---|
| Haut 2018 | PMR | 3 months | Low | -17.3 | 58.9 | 32 | -20.9 | 55.8 | 32 | 0.06 [-0.43, 0.55] |
| Puskarich 1992 | PMR | 8 weeks | High | 12.1 | 4.0 | 13 | 10.0 | 4.7 | 11 | 0.47 [-0.35, 1.28] |

Abbreviations: CI=confidence interval; N=study sample size; ROB=risk of bias; SD=standard deviation; SMD=standardized mean difference

Table 5 shows the COE for psychosocial therapy self-management interventions adapted for patients with epilepsy.

**Table 5. Certainty of Evidence for Psychosocial Therapy Self-management Interventions Adapted for Patients with Epilepsy**

| Outcome | Number of Studies (Patients) | Findings | Certainty of Evidence (Rationale) |
|---|---|---|---|
| Epilepsy self-management | None | Not applicable | **Insufficient** |
| Quality of life | 3 randomized (187) | MD 6.64 higher<br>(2.51 to 10.77 higher) | **Low certainty** for improved quality of life<br>(rated down for serious ROB, imprecision) |
| Seizure rates | 3 randomized (106) | SMD range from 0.06 to 0.47 higher | **Low certainty** for no clinically important improvement<br>(rated down for serious ROB, imprecision) |

Abbreviations: MD=mean difference; SMD=standardized mean difference; ROB=risk of bias

## *Secondary Outcomes*

### *Self-efficacy*

A single randomized study with low ROB reported the effects of a psychosocial therapy self-management intervention on self-efficacy.[52] This multicomponent intervention showed a small to moderate improvement in self-efficacy (SMD 0.37; 95% CI -0.04 to 0.78) at 6-months follow-up, but the confidence interval includes no effect.

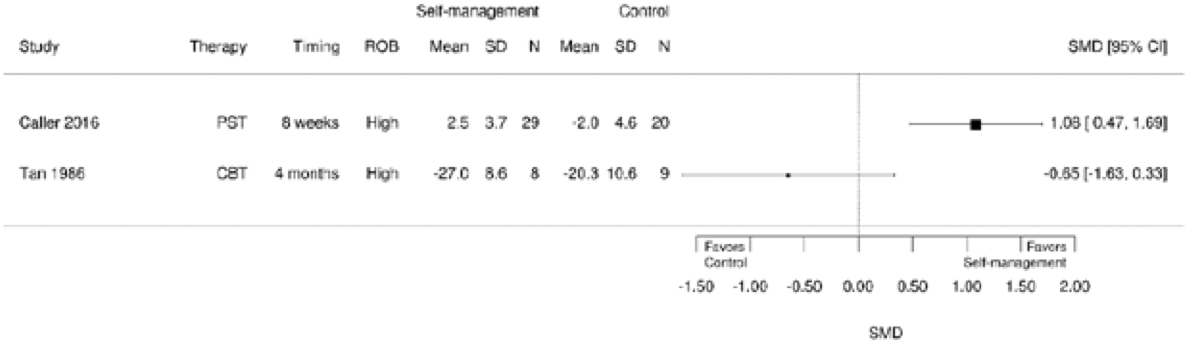
### *Social Function*

Two small randomized studies with high ROB reported conflicting effects on social function. Compared with usual care, the HOBSCOTCH intervention using problem-solving therapy with or without cognitive training showed improved social function (SMD 1.08; 95% CI 0.47 to 1.69; Figure 9) at 8 weeks.[46] In contrast, a small, high ROB study comparing CBT with supportive counseling and waitlist controls found no benefit on social function at 4-month follow-up (Figure 9).[56] A third study that compared 2 active interventions, CBT plus education to relaxation therapy, found no differential effect on social function (SMD 0.15; 95% CI -0.79 to 0.50).[54]

### *Medication Adherence*

Two studies reported effects on medication adherence using self-report measures. Neither a multicomponent self-management intervention[52] nor a CBT intervention [56] showed an effect on medication adherence at 4-6 months' follow-up. However, both studies were relatively small and the confidence interval included the possibility of a moderate effect.

**Figure 9. Effects of Psychosocial Therapy Self-management Interventions on Secondary Outcomes**



Abbreviations: CI=confidence interval; N=study sample size; ROB=risk of bias; SD=standard deviation; SMD=standardized mean difference

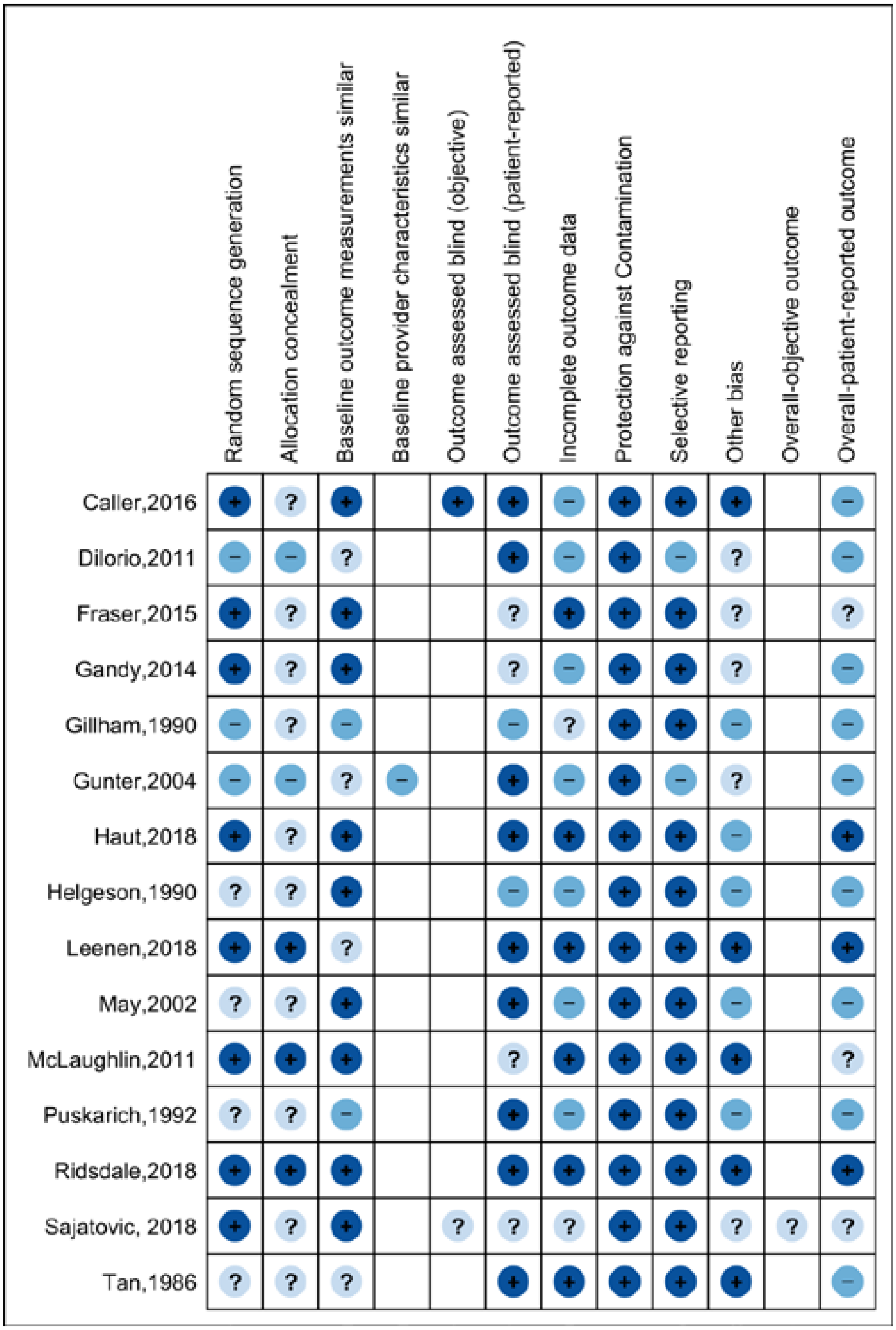
## Effects of Interventions on Other Outcomes

None of the studies evaluating therapy-based self-management interventions reported effects on safety outcomes or emergency department visits related to epilepsy.

## Quality of Evidence for KQ 1 and KQ 2 Studies

For the 13 randomized studies, the ROB for patient-reported outcomes was judged low for 3 studies,[50,52,57] unclear for 3 studies,[48,54,58] and high for 7 studies.[46,47,49,51,53,55,56] Objective outcomes (*eg*, emergency department visits) were not reported. Patterns that led to judgments of higher ROB included (1) inadequate or unclear allocation concealment (n=10), (2) incomplete outcome data (n=6), and (3) outcome assessments that did not clearly blind to intervention assignment (n=5). In addition to the lack of randomization for the 2 nonrandomized trials, unbalanced provider characteristics, incomplete outcome data, and possible selective outcome reporting led to a judgement of high ROB. ROB ratings for each study are shown in Figure 10 and the pattern of ROB assessments across studies in Figure 11.

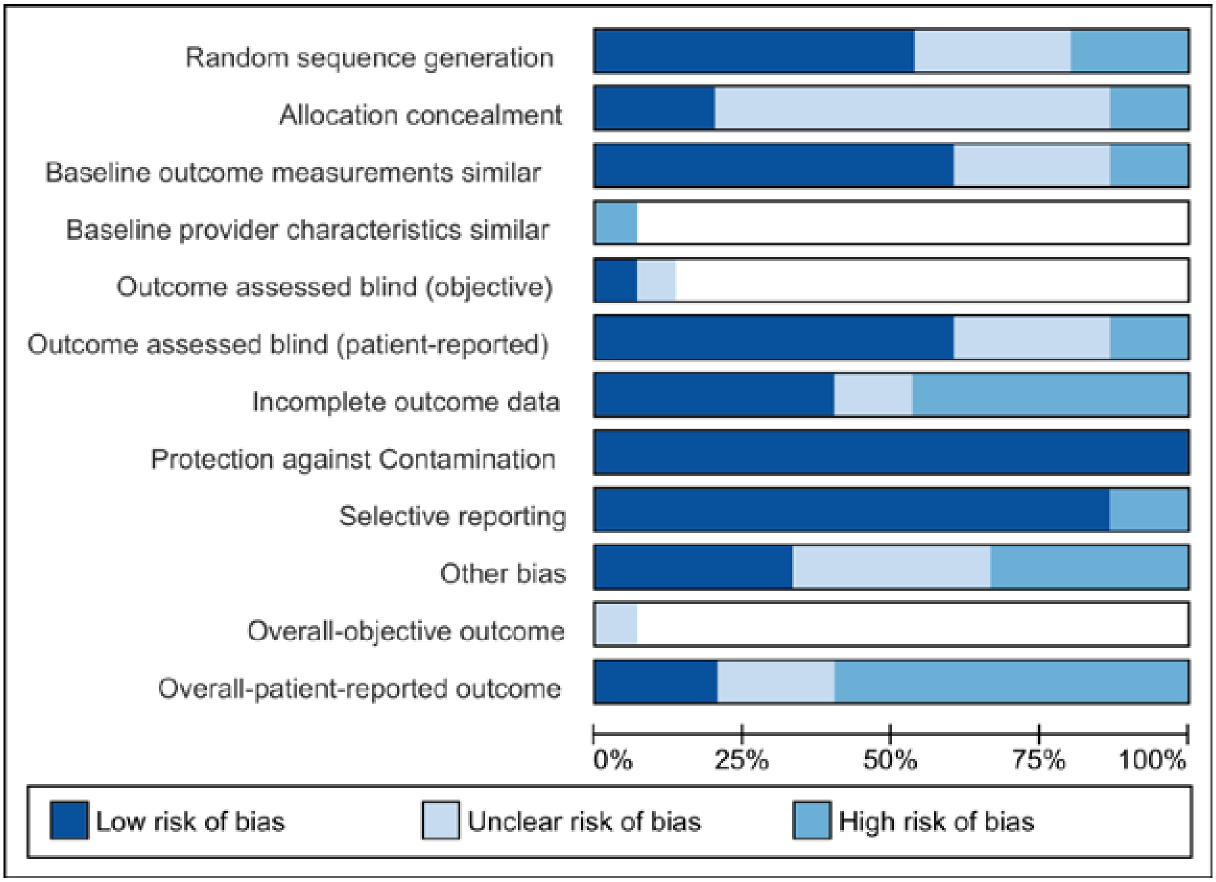
**Figure 10. Risk of Bias Ratings for the Included Studies**[a]



| | Random sequence generation | Allocation concealment | Baseline outcome measurements similar | Baseline provider characteristics similar | Outcome assessed blind (objective) | Outcome assessed blind (patient-reported) | Incomplete outcome data | Protection against Contamination | Selective reporting | Other bias | Overall-objective outcome | Overall-patient-reported outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Caller,2016 | + | ? | + | | + | + | − | + | + | + | | − |
| Dilorio,2011 | − | − | ? | | | + | − | + | − | ? | | − |
| Fraser,2015 | + | ? | + | | | ? | + | + | + | ? | | ? |
| Gandy,2014 | + | ? | + | | | ? | − | + | + | ? | | − |
| Gillham,1990 | − | ? | − | | | − | ? | + | + | − | | − |
| Gunter,2004 | − | − | ? | − | | + | − | + | − | ? | | − |
| Haut,2018 | + | ? | + | | | + | + | + | + | − | | + |
| Helgeson,1990 | ? | ? | + | | | − | − | + | + | − | | − |
| Leenen,2018 | + | + | ? | | | + | + | + | + | + | | + |
| May,2002 | ? | ? | + | | | + | − | + | + | − | | − |
| McLaughlin,2011 | + | + | + | | | ? | + | + | + | + | | ? |
| Puskarich,1992 | ? | ? | − | | | + | − | + | + | − | | − |
| Ridsdale,2018 | + | + | + | | | + | + | + | + | + | | + |
| Sajatovic, 2018 | + | ? | + | | ? | ? | ? | + | + | ? | ? | ? |
| Tan,1986 | ? | ? | ? | | | + | + | + | + | + | | − |

[a] White indicates items that were not applicable. Blue/positive indicates items that were judged low ROB. Light gray/question mark indicates items that were judged unclear ROB. Dark gray/negative indicates items that were judged high ROB.

**Figure 11. Risk of Bias Assessment Across Included Studies**[a]



[a] White indicates items that were not applicable.

## KEY QUESTION 3: What are the identified facilitators and barriers that impact the adoption of self-management interventions for adults with epilepsy in large-scale health systems such as the VA?

### Key Points

- Involving patients with epilepsy in the development of interventions may facilitate implementation by ensuring that the self-management content is relevant to living with epilepsy.
- Tailoring intervention content to each individual patient may facilitate implementation.
- Patients may have cognitive limitations that present a barrier to intervention engagement and adherence.
- Technology use for self-management is highly dependent on individual characteristics such as familiarity with and ownership of technological devices (*eg*, mobile phones, computers). More research is needed to identify best practices for technology-based self-management interventions for patients.

- The role of the clinician (*ie*, the individual who interacts with the patient to provide self-management education and support) is important to the implementation of the intervention. The clinician should be appropriately trained, have the duties of the intervention incorporated into their dedicated clinical time, and be provided with clearly written, standardized protocols that articulate the clinician interventionist's role in the intervention.
- No studies directly addressed facilitators and barriers to implementing and adopting self-management interventions for patients with epilepsy in the VHA or other large health systems.
- No studies directly enrolled Veterans with epilepsy.

## Detailed Findings

We present a summary of the studies, a description of identified themes across all studies, and the details for each theme organized by facilitators and barriers to implementation of self-management interventions. We identified 13 studies addressing facilitators and barriers to implementing self-management interventions for persons with epilepsy.[62-73] The study designs in this analysis included semi-structured interview (n=5),[65,67-69,73] cross-sectional survey (n=5),[64,70-72,74] longitudinal survey (n=1),[63] mixed-methods including group semi-structured interview, cross-sectional survey, and records review (n=1),[66] and discrete choice experiment (n=1).[62] Study respondents included patients with epilepsy, caregivers, and health care clinicians together,[63,64,66,68] patients and caregivers only,[62,65,67,69,70,72,73] and health care clinicians.[71] No studies were completed at the VHA, and none purposely recruited Veterans with epilepsy or stated they included Veterans with epilepsy.

### *Ecological Levels*

For each facilitator and barrier, we first identified the respondent (*eg*, the patient with epilepsy, caregiver, or health care clinician) associated with each theme. Then we examined each theme at 1 of 3 levels, adapted from ecological models of health behavior, which emphasize that determinants of behavior derive from individuals and characteristics of their environments that influence behavior directly and in interaction with one another.[36]

- Person level: Patient or caregiver who is engaging in the epilepsy self-management intervention
- Program level: Self-management intervention being implemented and evaluated
- Site/system level: Health care site or system where the self-management intervention is being implemented and evaluated

### *Themes*

Thematic synthesis of the abstracted data identified 5 themes across all KQ 3 studies that could be applied conceptually to facilitators and barriers. Table 6 defines the themes and Table 7 shows the presence of themes by study.

### Table 6. Themes Across Studies of Self-management of Epilepsy

| Theme | Definition |
|---|---|
| **Relevance** | Relevance of intervention content or topics that facilitate the acquisition of self-management skills in patients with epilepsy |
| **Personalization** | Intervention components that account for the individual social, physical, and environmental characteristics of the patient |
| **Intervention components** | Components and dosing of the intervention |
| **Technology considerations** | Considerations that account for patient's use of, familiarity with, and ownership of technology (*eg*, computers, laptops, mobile phones) |
| **Clinician interventionist** | Role and preparation of individual who leads the intervention, engages with the patient, and provides self-management education and/or support to the patient |

### Table 7. Presence of Themes by Study

| Study | Facilitators | | | | | Barriers | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | R | P | IC | TC | CI | R | P | IC | TC | CI |
| Atkinson-Clark, 2018[62] | | | | | | | X | X | | |
| Begley, 2015[63] | | | X | X | | | | X | | |
| Buelow, 2001[73] | X | | | | | | | | | |
| Clark, 2010[71] | X | | | | | X | X | | | X |
| Fraser, 2011[72] | X | | X | | X | | | | | |
| Johnson, 2012[64] | | | | | | X | | | | X |
| Laybourne, 2015[65] | X | X | X | | | | | X | | |
| Leenen, 2016[70] | | X | | X | | | X | | X | |
| Leenen, 2017[66] | | | X | | | X | X | X | X | X |
| Ridsdale, 2017[67] | | | X | | | X | X | X | | |
| Snape, 2017[68] | X | X | X | | | | | X | | |
| Walker, 2012[69] | | X | | | | | X | | | |
| Begley, 2018[74] | X | | X | X | | | | | X | |

Abbreviations for themes (from Table 6): R=Relevance; P=Personalization; IC=Intervention components; TC=Technology considerations; CI=Clinician interventionist

## Facilitators

The presence of facilitators of epilepsy self-management interventions at any level (*ie*, person, program, site/system) was noted in 10 studies.[63,65-73] Two studies did not include any facilitators.[62,64]

### *Relevance*

At the person level, facilitators included the opportunity for the patient with epilepsy to acquire self-management skills and content that were highly applicable to living with epilepsy (*eg*, eliciting concerns about self-managing and daily living from the patient or caregiver)[68,71,74] and the participant's desires for obtaining self-management skills from the intervention.[73,74] Facilitators at the program level included intentional programmatic features such as enabling the patient's acquisition of skills for living with epilepsy, learning how to apply self-management skills and coping strategies in daily life, and communicating with family, caregivers, and health care clinicians about epilepsy.[65,68,72] No relevance facilitators were identified at the site/system level.

### *Personalization*

At the person level, facilitators included identifying whether the patient owned the necessary technology for the intervention (*eg*, computer, mobile telephone)[70] and had an identified source of social support,[69] and whether the intervention was congruent with the patient's preference for peer support or group interaction.[65,68] At the program level, facilitators included developing the intervention and tailoring its components to build on the current self-management practices of the patient.[70,74] No personalization facilitators were identified at the site/system level.

### *Intervention Components*

At the person level, facilitators included providing written materials (*eg*, educational content) to the patient or caregiver during and after the intervention.[68] At the program level, facilitators included involving family members in the intervention,[66] using an empowerment approach to help the patient develop self-management skills,[65,74] the format of the intervention (*eg*, group format that included both the patient and caregiver),[68] the ability to personalize materials to each patient,[68,72,74] the availability of written materials,[63,65,68] the ability to interact with a group,[66,67] the provision of peer support,[66,67] and the length and duration of the intervention sessions.[66,67] At the site/system level, facilitators included developing intervention materials using uniform program standards to ensure program fidelity across intervention sites.[68] One study indicated that the site of the intervention (*ie*, medical center) was unimportant, as patients with epilepsy indicated no preference of one site over another.[72]

### *Technology Considerations*

At the program level, facilitators included the high level of usability of intervention components located on the internet, mobile applications, or phones.[63,70,74] No technology facilitators were identified at the person or site/system levels.

### *Clinician Interventionist*

At the program level, facilitators included creating an intervention team consisting of a patient in tandem with an expert health care clinician who could deliver the intervention content.[72] No clinician interventionist facilitators were identified at the person or site/system levels.

## Barriers

The presence of barriers to epilepsy self-management interventions at any level was noted in 10 studies.[62-71] Two studies did not include any relevant barriers.[72,73] Stakeholders included clinicians, social service providers, and researchers,[71] and patients and clinicians.[64]

### *Relevance*

At the program level, barriers included incongruent responses between patients and clinicians about the patient's problems and needs to be addressed in the epilepsy self-management program,[64] incongruent opinions by clinicians, researchers, and social service providers on the necessary intervention content,[71] incongruent responses between patients and clinicians on who should lead the intervention and provide epilepsy self-management education and support,[64] educational content that was too general or lacking in personalization or tailoring to the patient, his or her disease state and relevant comorbidities,[64,67,74] and not identifying what the patient views as important in self-management and living with epilepsy.[66] No relevance barriers were identified at the person or site/system levels.

### *Personalization*

At the person level, barriers included the patient's memory and/or cognitive impairments,[62,64,67,68,70,71] the patient's disinterest in participating in a self-management intervention,[62] not identifying the patient's preference or desire for self-management support,[69] and no current use of the technology by the patient.[70] At the program level, barriers included not accounting for the cognitive limitations of patient.[67] At the site/system level, barriers included not accounting for the characteristics of the patient population such as the patient's access to health care[71] or transportation concerns.[66]

### *Intervention Components*

At the program level, barriers included requiring the patient to incur a cost for participating in the intervention,[62] not identifying how demographics (*eg*, country of origin, burden of disease, socioeconomic status, level of activation) influence the patient's participation and views of the intervention,[62] not identifying the ideal time for follow-up by the clinician after the intervention,[66] not having clear instructions for the role of caregivers participating in or affected by the intervention,[66] not having written materials (*eg*, program manuals, handouts, website resources) the patient can refer to during and after the intervention,[65,66] having groups heterogeneously composed of individuals with disparate experiences of living with epilepsy,[67] experiencing challenges to scheduling group intervention sessions because of calendar conflicts for participants and clinicians,[68] and not identifying the optimal duration and length of the intervention for patients.[62,65,67] Barriers at the site/system level included having different levels of attrition at study sites[63] and challenges to using a participatory approach to intervention development and content identification (*eg*, lengthy time to complete, need to obtain ethical approval, and efforts to ensure participant engagement).[68] No intervention component barriers were identified at the person level.

### *Technology Considerations*

At the person level, barriers included the patient's lack of knowledge about eHealth tools and functions, having concerns about the privacy of eHealth tools, and varying individual preferences for using technology for epilepsy self-management.[70] At the program level, barriers included difficulty developing eHealth tools with high usability, and a lack of help for users encountering technical difficulties.[66,70,74] At the site/system level, barriers included not acknowledging or addressing the inequity of access to eHealth tools within the sample or the person with epilepsy's concerns about the privacy of eHealth tools.[70]

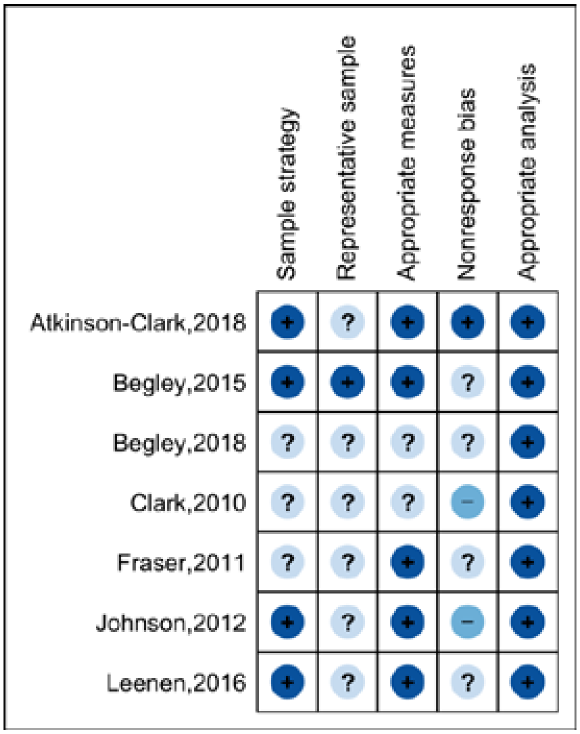
### *Clinician Interventionist*

At the program level, barriers included not incorporating the duties of the intervention into the clinician interventionist's normal job duties,[66] not adequately preparing the clinician interventionist to deliver the intervention content,[66] developing a complex intervention protocol that is difficult to deliver,[66] and not identifying the optimal professional role and educational training of the clinician interventionist.[64,71] At the site/system level, barriers included a lack of opportunity for the clinician interventionist to engage in continuity of care for the person with epilepsy following the conclusion of the intervention,[66] and not accounting for the limited time allotted for medical visits.[71,74] No clinician interventionist barriers were identified at the person level.

## Quality of Evidence for KQ 3 Studies

The tools used to assess risk of bias (ROB) for the descriptive quantitative, mixed-methods, and qualitative studies did not provide for the calculation of summary scores for individual papers. Among the 7 descriptive quantitative studies,[62-64,70-72,74] ROB was heterogeneous (Figure 12). Patterns that led to judgments of higher ROB included unclear representativeness of the sample (n=6),[62,64,70-72,74] high (n=2)[64,71] or unclear (n=4)[63,70,72,74] ROB from non-response, unclear risk of bias in sampling strategy (n=3),[71,72,74] and unclear appropriateness of measures (n=2).[71,74]

**Figure 12. Risk of Bias Ratings for the Included Descriptive Quantitative Studies[a]**

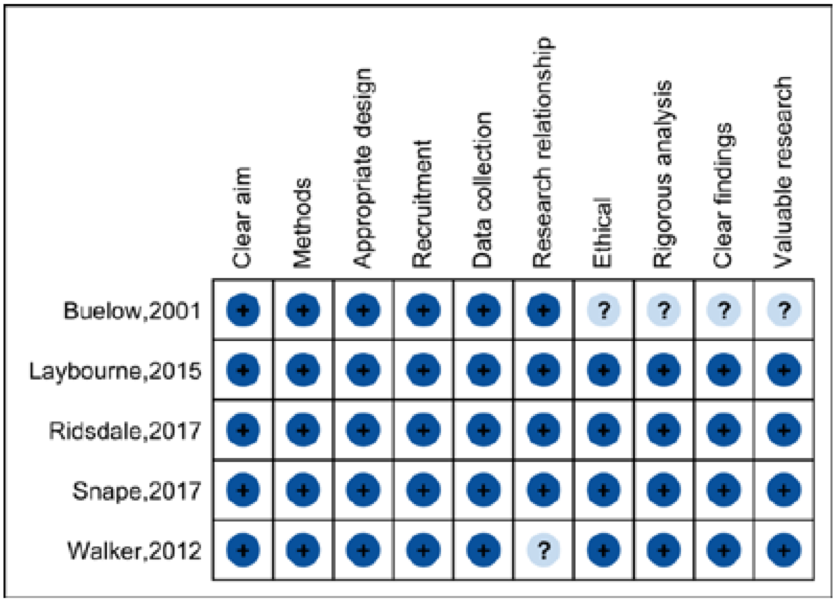


| | Sample strategy | Representative sample | Appropriate measures | Nonresponse bias | Appropriate analysis |
|---|---|---|---|---|---|
| Atkinson-Clark,2018 | + | ? | + | + | + |
| Begley,2015 | + | + | + | ? | + |
| Begley,2018 | ? | ? | ? | ? | + |
| Clark,2010 | ? | ? | ? | − | + |
| Fraser,2011 | ? | ? | + | ? | + |
| Johnson,2012 | + | ? | + | − | + |
| Leenen,2016 | + | ? | + | ? | + |

[a] Blue/positive indicates items that were judged low ROB. Light gray/question mark indicates items that were judged unclear ROB. Dark gray/negative indicates items that were judged high ROB.

The overall ROB in the 5 qualitative studies was low (Figure 13).[65,67-69,73] However, we identified several concerning flaws in 1 study[73] including insufficient information provided regarding ethical considerations or consideration of the relationship between the researcher and participants, a lack of rigorous analysis of study findings, and no description of the clear value of the research. We also identified 1 study that had unclear ROB regarding the relationship of the researcher to the participants.[69]

### Figure 13. Risk of Bias Ratings for the Included Qualitative Studies[a]

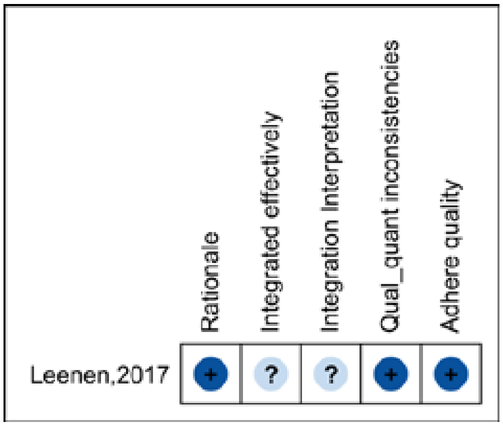


| | Clear aim | Methods | Appropriate design | Recruitment | Data collection | Research relationship | Ethical | Rigorous analysis | Clear findings | Valuable research |
|---|---|---|---|---|---|---|---|---|---|---|
| Buelow,2001 | + | + | + | + | + | + | ? | ? | ? | ? |
| Laybourne,2015 | + | + | + | + | + | + | + | + | + | + |
| Ridsdale,2017 | + | + | + | + | + | + | + | + | + | + |
| Snape,2017 | + | + | + | + | + | + | + | + | + | + |
| Walker,2012 | + | + | + | + | + | ? | + | + | + | + |

[a] Blue/positive indicates items that were judged low ROB. Gray/question mark indicates items that were judged unclear ROB.

The ROB of the mixed-methods study was somewhat unclear, as it had no integration of its qualitative and quantitative findings (Figure 14).[66]

### Figure 14. Risk of Bias Ratings for the Included Mixed-Methods Study[a]



| | Rationale | Integrated effectively | Integration Interpretation | Qual_quant inconsistencies | Adhere quality |
|---|---|---|---|---|---|
| Leenen,2017 | + | ? | ? | + | + |

[a] Blue/positive indicates items that were judged low ROB. Gray/question mark indicates items that were judged unclear ROB.

# SUMMARY AND DISCUSSION

We evaluated self-management interventions for patients with epilepsy, examining effects on a range of outcomes of importance to patients, clinicians, and policymakers. Our review is unique in its use of a standard definition for self-management, focus on high-quality study designs, and rigorous analysis of studies that address facilitators and barriers to implementation and adoption of self-management interventions. We identified 15 studies addressing the effects of self-management and 13 studies that addressed implementation and adoption. Only 1 specifically included Veterans. We identified 2 broad categories for self-management interventions: (1) educationally focused interventions created for patients with epilepsy, where skill acquisition was often implicitly targeted in the process, and (2) established psychosocial therapies such as CBT that were adapted for people with epilepsy, where the educational component was often implicit. We found limited evidence for benefit on a priori selected primary or secondary outcomes. Educational self-management interventions may improve the use of self-management practices, and quality of life may improve with therapy-based self-management approaches. There was low to moderate certainty of no improvement in seizure rates across self-management interventions. Sparse evidence suggested possible benefit of psychosocial therapy interventions on self-efficacy. Effects on employment and health care utilization were not reported.

Studies of barriers and facilitators to implementation and adoption of epilepsy self-management interventions addressed factors primarily at the patient level or program level. No studies directly addressed implementation and adoption issues for large health systems such as the VHA. Important themes that could inform the development, implementation, and/or adoption of future self-management interventions included (1) the desire of patients with epilepsy to be involved in the development of intervention content, (2) recognition that cognitive limitations may affect engagement and adherence, and (3) the need for clinicians who are appropriately trained to provide self-management interventions and whose job function specifically includes this role.

Previous literature reviews have focused narrowly on group-based interventions,[43] single therapeutic techniques,[42] or interventions such as those to improve antiepileptic drug adherence[38] that would not meet standard definitions for self-management. Others have addressed self-management interventions for individuals with chronic health conditions more generally,[39,44,75] and diverse approaches including care delivery redesigns.[24,41] None addressed implementation issues. A rapid synthesis of 30 prior systematic reviews for long-term conditions (LTCs) concluded “Supporting self-management is inseparable from the high-quality care for LTCs.”[44] Consistent with our findings, authors of prior reviews that focused on epilepsy found limited evidence to support an effect on the outcomes of interest other than epilepsy self-management. Some reviews reported benefit for outcomes (*eg*, emotional well-being) that we did not consider.[43] Previous review authors noted that findings were limited by unclear risk of bias, non-reporting of intervention fidelity, and heterogeneity of outcome measures observed across studies. Across these previous reviews, no single intervention was found to be consistently effective across all outcomes of interest. In contrast to our study, these reviews elected not to perform meta-analyses because of the diversity of study designs (randomized and nonrandomized), interventions, and in some cases, patient populations. We established study eligibility criteria that narrowed the scope of eligible studies and conducted limited meta-analyses of randomized trials by intervention category. We think these summary estimates facilitate understanding of intervention effects.

# CLINICAL AND POLICY IMPLICATIONS

Self-management of chronic illness that is aligned with an individual's values and preferences is considered an important component in delivering patient-centered care in the VHA,[76,77] and is a pillar of VHA's Patient Aligned Care Teams (PACT).[78] Outside of the VHA, Medicare covers self-management services for patients with diabetes mellitus only,[79] but for other chronic conditions, services are covered only within the context of chronic disease management programs for multiple chronic diseases.[80]

For patients with epilepsy, the Institute of Medicine (IOM) in 2012 recommended "access to relevant and usable knowledge … to achieve optimal self-management of their epilepsy"[15] and that these resources allow for tailoring to individual needs. Further, the IOM recommended that research be devoted to "evaluating, replicating, and expanding the use of epilepsy self-management programs."[15] This recommendation was based on a careful review of evidence by a multidisciplinary panel but did not include a formal systematic review. Our protocol-driven review addresses the IOM mandate to evaluate existing research and may be of broader interest to epilepsy centers and patient advocacy groups interested in following IOM recommendations to expand epilepsy self-management programs. We found that epilepsy self-management interventions varied widely in duration, format, and resource requirements. While no intervention demonstrated improvements in medication adherence or self-reported seizure frequency, limited data suggested the psychoeducational programs PACES and MOSES improved self-management skills in people with epilepsy. These group-based programs provided 10-16 hours of in-person training and were delivered by clinicians and/or peers with special training in epilepsy self-management. Implementing programs such as these in VHA would require considerable resources in the form of dedicated clinical staff, trained peer leaders, and identified meeting space. There also may be too few patients to efficiently form groups outside of urban centers or VA Epilepsy Centers of Excellence (ECoE).

The VA ECoE is a network of 16 Centers that provide comprehensive care to Veterans with seizure disorders. These Centers have adopted quality measures addressing self-management through their implementation of the Quality Indicators in Epilepsy Treatment (QUIET) tool.[81] The QUIET measure set includes medication compliance assessment/enhancement and annual screening of self-management skills (side effect monitoring, contraception, mood disorders, lifestyle triggers, safety). Uniform clinical templates are available to address some of these measures, but individual ECoE sites and providers have flexibility in implementation, and patient education approaches are not standardized.

Our review addressed outcomes important to decision-making but should be considered as only one input into any decision about implementing and adopting self-management interventions that provide education and support more broadly for patients with epilepsy and their caregivers. Other outcomes, such as effects on patient experience and emotional well-being, may be important. Resources required to implement effective programs, whether to provide services to all or targeted to patients with epilepsy, and competing quality improvement initiatives should be considered. If the VHA were to move to implement and adopt self-management services for patients with epilepsy through the ECoE network or more broadly through PACT, our description of intervention components and synthesis of implementation and adoption barriers and facilitators could inform that effort. Clinician interventionists would benefit from intervention-specific training, dedicated time, and appropriate funding dedicated to providing self-management education and support, as opposed to layering on intervention responsibilities as a marginal service. Intervention materials should be personalized to the individual patient with epilepsy and include written information, and should be available before, during and after intervention sessions. A greater emphasis on goal-setting,[82] a core feature of behavioral change interventions, should be considered. Delivery methods may vary, but should include consideration for web or app-based interventions[83]; if delivery is face-to-face with a clinician interventionist, dedicated space and salary support should be addressed. Introducing new care approaches into clinical care is often challenging. However, the VHA is uniquely situated to take on this challenge through the Quality Enhancement Research Initiative (QUERI) program,[84] whose mission is to advance implementation science and identify effective strategies for implementing effective interventions.

The studies included in this review varied widely in their design, statistical analysis, and reporting. We highlight the most recent study included in the review, the SMART intervention by Sajatovic and colleagues, as an example of a well-structured and -reported study. Notable features of this study were the inclusion of Veteran populations, the inclusion of health care utilization and safety outcomes which were not reported in other studies we reviewed, and reporting that was transparent and amenable to meta-analysis. Future investigators should consider the SMART trial as a model for study design and sources of research support could use it as a guide for funding subsequent work in epilepsy self-management.

## LIMITATIONS

Our review benefited from being protocol driven, leveraging input from an expert panel, using a conceptual model, conducting an updated literature search that identified recent studies not included in prior reviews, using rigorous qualitative methods for analyzing barriers and facilitators to implementation and adoption, and using a detailed approach to categorizing and defining self-management intervention components. Despite these strengths, limitations in our approach and the primary literature remain. For example, we excluded studies that required a depression diagnosis or elevated depressive symptoms for enrollment, and thus studies with a depression-specific focus (*eg*, Project Uplift[85]) were excluded. Other limitations are detailed below.

### Publication Bias

Given the small number of studies, statistical methods to detect publication bias are not useful. Other strategies, such as searching ClinicalTrials.gov for completed but unpublished studies is not a particularly effective way to identify publication bias.[86] Thus, although no publication bias was detected, tools for detection are poor.

### Study Quality

We were also limited by the existing literature. We identified relatively few studies, most with enrollment of fewer than 100 patients, and most were assessed as unclear or high ROB. Inadequate or unclear allocation concealment, incomplete outcome data, and outcome assessments that were not clearly blinded to intervention assignment contributed to judgments of higher risk. Interventions were often described incompletely. Intervention fidelity was often not reported; for many of the psychosocial therapy interventions, an educational component was only inferred, not described explicitly. Some outcomes of interest, such as effects on employment or workplace productivity and health care utilization were not reported. Other self-reported outcomes, in particular seizure rates, are difficult to measure. The tools used to assess the risk of bias for the studies included in KQ 3 did not allow for the calculation of summary scores. However, we assessed all studies for ROB. Of the 13 studies included in KQ 3, only 1 exhibited a high ROB due to insufficient information about ethical concerns, lack of rigorous analysis of study findings, and no clear value of the research. The remaining KQ 3 studies exhibited either low or unclear ROB.

### Heterogeneity

Self-management is a complex intervention, and these types of interventions make synthesis challenging. We compared interventions that varied in study design, intervention approaches, and patients enrolled. We addressed this diversity, in part, by separately analyzing randomized and nonrandomized trials and by considering intervention category. We described, but did not address quantitatively, variability due to differences in intervention designs such as intensity, delivery mode, and goals. Despite variability in intervention design characteristics, effects on most outcomes were consistent. For the studies in KQ 3, we addressed the inherent diversity by identifying the respondent (*eg*, patient with epilepsy, caregiver, or clinician) and then synthesizing emerging themes within ecological levels.

### Applicability of Findings to the VA Population

Only 1 of the included studies was conducted in the VHA or specifically with Veterans. However, we limited eligibility to studies conducted in OECD countries, which improves applicability to VHA. All intervention studies were conducted in North America, Europe, or Australia. Identified studies included predominantly white samples, and mid-life patients (median age 40) in contrast to the >50% of Veterans with epilepsy who are age 65 or older. Although this approach improved applicability of findings to Veterans, it means that potentially relevant studies conducted in non-OECD countries were excluded.

## RESEARCH GAPS/FUTURE RESEARCH

We structure our reflection of gaps in evidence by considering each element of the PICOTS framework (Table 8). Although it would be possible to generate an extensive list of gaps in evidence, we restricted this list to the areas judged to be highest priority, given the current state of evidence. To facilitate future literature syntheses, we encourage investigators conducting clinical trials to include these studies in trial registries.

**Table 8. Highest Priority Evidence Gaps**

| PICOTS Domain | Evidence Gap |
|---|---|
| **Population** | Research is needed with patients who are earlier in their course of illness and studies specifically focused on older adults with epilepsy. Evaluation of interventions and barriers/facilitators to implementation and adoption of self-management interventions with Veterans and in large health systems is missing. |
| **Interventions** | · Self-management interventions are needed that incorporate patient, caregiver, and clinician interventionist input, account for cognitive limitations, incorporate peer support, and address other barriers to engagement and adherence. |

| PICOTS Domain | Evidence Gap |
|---|---|
| | · The role of technology (*eg*, smartphones, web-based support) has not been well studied in patients with epilepsy.<br>· Patients with epilepsy expressed a desire for an intervention team composed of a person with epilepsy and a clinician interventionist to provide self-management education and support. Future research should further examine the composition of this interventionist dyad and identify who the clinician interventionist should be (*eg*, registered nurse, advanced practice registered nurse, physician, physician assistant).<br>· Future research should focus on the extent to which these intervention components (*eg*, peer support), use of technology, and other identified barriers/facilitators influence the person with epilepsy's initial and sustained engagement in an epilepsy self-management program. |
| **Comparators** | Active controls, including usual care, are appropriate and should be described carefully. |
| **Outcomes** | · With the exception of quality of life, outcome measures varied greatly across studies, making synthesis difficult.<br>· Research is needed on outcomes most valued by patients with epilepsy, and how to best measure these outcomes.<br>· Future research is needed that specifically addresses the implementation and adoption of epilepsy self-management programs, as there may be additional personal, program, and site/system level barriers that need to be identified and addressed. |
| **Timing** | Self-management skills can take time to master and may take longer for patients with cognitive difficulty. Studies varied greatly in the timing of outcomes assessments. Consensus, or research, on the time required to acquire self-management skills and the time required for new skills to potentially improve clinical outcomes should inform the timing of outcome assessments. |
| **Setting** | Few studies have examined interventions delivered outside of clinical settings. Future research should determine the preferred location for a self-management program for patients with epilepsy and their caregivers. |

## CONCLUSIONS

Epilepsy is one of the most common chronic neurological conditions, with the potential to generate significant morbidity, impaired quality of life, socioeconomic decline, and high health care costs. Self-management is essential for patients who live with a chronic disease, and the VHA and other health systems are interested in offering self-management training to patients with epilepsy. In our protocol-based review, we found that tested interventions broke down into 2 categories: educational and psychosocial therapy interventions. These self-management interventions showed clinically important benefit for only a limited number of outcomes, but the confidence in these findings was mostly low. Further, there is unexplained variability in the effect of education interventions on quality of life and self-efficacy. Findings on facilitators and barriers to the implementation were stronger and point to a clearer path to the design and adoption of self-management interventions, including factors of patient personalization, information delivery, use of technology, and intervention personnel. Future research should be designed to address these implementation issues, and should include standardized outcome measures prioritized by patients and other stakeholders and Veteran populations.

# REFERENCES

1. World Health Organization. Improving Access to Epilepsy Care. Available at: https://www.who.int/mental_health/neurology/epilepsy/en/. Accessed December 20, 2018.
2. Rehman R, Kelly PR, Husain AM, et al. Characteristics of Veterans diagnosed with seizures within Veterans Health Administration. *J Rehabil Res Dev*. 2015;52(7):751-62.
3. Kanner AM. Management of psychiatric and neurological comorbidities in epilepsy. *Nat Rev Neurol*. 2016;12(2):106-16.
4. Nevalainen O, Ansakorpi H, Simola M, et al. Epilepsy-related clinical characteristics and mortality: a systematic review and meta-analysis. *Neurology*. 2014;83(21):1968-77.
5. Thurman DJ, Logroscino G, Beghi E, et al. The burden of premature mortality of epilepsy in high-income countries: A systematic review from the Mortality Task Force of the International League Against Epilepsy. *Epilepsia*. 2017;58(1):17-26.
6. Liporace J, D'Abreu A. Epilepsy and women's health: family planning, bone health, menopause, and menstrual-related seizures. *Mayo Clin Proc*. 2003;78(4):497-506.
7. Smaldone M, Sukkarieh T, Reda A, et al. Epilepsy and erectile dysfunction: a review. *Seizure*. 2004;13(7):453-9.
8. Morrell MJ. Stigma and epilepsy. *Epilepsy Behav*. 2002;3(6S2):21-25.
9. Tian N, Boring M, Kobau R, et al. Active epilepsy and seizure control in adults - United States, 2013 and 2015. *MMWR Morb Mortal Wkly Rep*. 2018;67(15):437-442.
10. Buck D, Baker GA, Chadwick DW, et al. Factors influencing compliance with antiepileptic drug regimes. *Seizure*. 1997;6(2):87-93.
11. Farooq S, Naeem F. Tackling nonadherence in psychiatric disorders: current opinion. *Neuropsychiatr Dis Treat*. 2014;10:1069-77.
12. U.S. Centers For Disease Controls and Prevention Epilepsy Program. About one-half of adults with active epilepsy and seizures have annual family incomes under $25,000: The 2010 and 2013 US National Health Interview Surveys. *Epilepsy Behav*. 2016;58:33-4.
13. Samsonsen C, Reimers A, Brathen G, et al. Nonadherence to treatment causing acute hospitalizations in people with epilepsy: an observational, prospective study. *Epilepsia*. 2014;55(11):e125-8.
14. Devinsky O, Ryvlin P, Friedman D. Preventing sudden unexpected death in epilepsy. *JAMA Neurol*. 2018;75(5):531-532.
15. Institute of Medicine. Epilepsy Across the Spectrum: Promoting Health and Understanding. 2012. Available at: https://www.nap.edu/catalog/13379/epilepsy-across-the-spectrum-promoting-health-and-understanding. Accessed October 22, 2018.
16. Coleman K, Austin BT, Brach C, et al. Evidence on the Chronic Care Model in the new millennium. *Health Aff (Millwood)*. 2009;28(1):75-85.
17. Davy C, Bleasel J, Liu H, et al. Effectiveness of chronic care models: opportunities for improving healthcare practice and health outcomes: a systematic review. *BMC Health Serv Res*. 2015;15:194.
18. Franek J. Self-management support interventions for persons with chronic disease: an evidence-based analysis. *Ont Health Technol Assess Ser*. 2013;13(9):1-60.
19. Jackson GL, Powers BJ, Chatterjee R, et al. Improving patient care. The patient centered medical home: a systematic review. *Ann Intern Med*. 2013;158(3):169-78.

20. Center for Medicare & Medicaid Innovation. Comprehensive Primary Care Plus. Innovation Models. Available at: https://innovation.cms.gov/initiatives/Comprehensive-Primary-Care-Plus. Accessed May 17, 2018.
21. Barlow J, Wright C, Sheasby J, et al. Self-management approaches for people with chronic conditions: a review. *Patient Educ Couns*. 2002;48(2):177-87.
22. Warsi A, Wang PS, LaValley MP, et al. Self-management education programs in chronic disease: a systematic review and methodological critique of the literature. *Arch Intern Med*. 2004;164(15):1641-9.
23. Schaffler J, Leung K, Tremblay S, et al. The effectiveness of self-management interventions for individuals with low health literacy and/or low income: a descriptive systematic review. *J Gen Intern Med*. 2018;33(4):510-523.
24. Bradley PM, Lindsay B, Fleeman N. Care delivery and self management strategies for adults with epilepsy. *Cochrane Database Syst Rev*. 2016;2:CD006244.
25. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097.
26. Glasgow RE, Davis CL, Funnell MM, et al. Implementing practical interventions to support chronic illness self-management. *Jt Comm J Qual Saf*. 2003;29(11):563-74.
27. Jonkman NH, Schuurmans MJ, Jaarsma T, et al. Self-management interventions: proposal and validation of a new operational definition. *J Clin Epidemiol*. 2016;80:34-42.
28. Cochrane Effective Practice and Organisation of Care (EPOC). Suggested risk of bias criteria for EPOC reviews. EPOC Resources for review authors, 2017. Available at: http://epoc.cochrane.org/resources/epoc-resources-review-authors Accessed May 17, 2018.
29. Evidence Partners Inc. DistillerAI website. Available at: https://www.evidencepartners.com/distiller-ai/. Accessed October 12, 2018.
30. Critical Appraisal Skills Programme (CASP). CASP Qualitative Checklist. Available at: http://www.casp-uk.net/casp-tools-checklists. Accessed May 17, 2018.
31. Hong QN, Pluye P, Fàbregues S, et al. Mixed Methods Appraisal Tool (MMAT), version 2018. Registration of Copyright (#1148552), Canadian Intellectual Property Office, Industry Canada. Available at: http://mixedmethodsappraisaltoolpublic.pbworks.com/w/page/127425845/Download%20the%20MMAT. Accessed October 11, 2018.
32. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. Hillsdale, NJ: Erlbaum; 1988.
33. Knapp G, Hartung J. Improved tests for a random effects meta-regression with a single covariate. *Stat Med*. 2003;22(17):2693-710.
34. Gale NK, Heath G, Cameron E, et al. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Med Res Methodol*. 2013;13:117.
35. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Med Res Methodol*. 2008;8:45.
36. Sallis JF, Owen N, Fisher E. Ecological Models of Health Behavior. In: Health behavior: Theory, Research, and Practice. 5th Edition. 2015:43-64.
37. Hultcrantz M, Rind D, Akl EA, et al. The GRADE Working Group clarifies the construct of certainty of evidence. *J Clin Epidemiol*. 2017;87:4-13.
38. Al-Aqeel S, Al-Sabhan J. Strategies for improving adherence to antiepileptic drug treatment in patients with epilepsy. *Cochrane Database Syst Rev*. 2011(1):Cd008312.

39. Beatty L, Lambert S. A systematic review of internet-based self-help therapeutic interventions to improve distress and disease-control among adults with chronic health conditions. *Clin Psychol Rev*. 2013;33(4):609-22.
40. Bradley PM, Lindsay B. Care delivery and self-management strategies for adults with epilepsy. *Cochrane Database Syst Rev*. 2008(1):Cd006244.
41. Edward KL, Cook M, Giandinoto JA. An integrative review of the benefits of self-management interventions for adults with epilepsy. *Epilepsy Behav*. 2015;45:195-204.
42. Gandy M, Sharpe L, Perry KN. Cognitive behavior therapy for depression in people with epilepsy: a systematic review. *Epilepsia*. 2013;54(10):1725-34.
43. Smith A, McKinlay A, Wojewodka G, et al. A systematic review and narrative synthesis of group self-management interventions for adults with epilepsy. *BMC Neurol*. 2017;17(1):114.
44. Taylor SJC, Pinnock H, Epiphaniou E, et al. A rapid synthesis of the evidence on interventions supporting self-management for people with long-term conditions: PRISMS - Practical systematic Review of Self-Management Support for long-term conditions. *Health Serv Deliv Res*. 2014;2:53.
45. O’Rourke G, O’Brien JJ. Identifying the barriers to antiepileptic drug adherence among adults with epilepsy. *Seizure*. 2017;45:160-168.
46. Caller TA, Ferguson RJ, Roth RM, et al. A cognitive behavioral intervention (HOBSCOTCH) improves quality of life and attention in epilepsy. *Epilepsy Behav*. 2016;57(Pt A):111-117.
47. DiIorio C, Bamps Y, Walker ER, et al. Results of a research study evaluating WebEase, an online epilepsy self-management program. *Epilepsy Behav*. 2011;22(3):469-74.
48. Fraser RT, Johnson EK, Lashley S, et al. PACES in epilepsy: Results of a self-management randomized controlled trial. *Epilepsia*. 2015;56(8):1264-74.
49. Gandy M, Sharpe L, Nicholson Perry K, et al. Cognitive behaviour therapy to improve mood in people with epilepsy: a randomised controlled trial. *Cogn Behav Ther*. 2014;43(2):153-66.
50. Haut SR, Lipton RB, Cornes S, et al. Behavioral interventions as a treatment for epilepsy: A multicenter randomized controlled trial. *Neurology*. 2018;90(11):e963-e970.
51. Helgeson DC, Mittan R, Tan SY, et al. Sepulveda Epilepsy Education: the efficacy of a psychoeducational treatment program in treating medical and psychosocial aspects of epilepsy. *Epilepsia*. 1990;31(1):75-82.
52. Leenen LAM, Wijnen BFM, Kessels AGH, et al. Effectiveness of a multicomponent self-management intervention for adults with epilepsy (ZMILE study): A randomized controlled trial. *Epilepsy Behav*. 2018;80:259-265.
53. May TW, Pfafflin M. The efficacy of an educational treatment program for patients with epilepsy (MOSES): results of a controlled, randomized study. Modular Service Package Epilepsy. *Epilepsia*. 2002;43(5):539-49.
54. McLaughlin DP, McFarland K. A randomized trial of a group based cognitive behavior therapy program for older adults with epilepsy: the impact on seizure frequency, depression and psychosocial well-being. *J Behav Med*. 2011;34(3):201-7.
55. Puskarich CA, Whitman S, Dell J, et al. Controlled examination of effects of progressive relaxation training on seizure reduction. *Epilepsia*. 1992;33(4):675-80.
56. Tan SY, Bruni J. Cognitive-behavior therapy with adult patients with epilepsy: a controlled outcome study. *Epilepsia*. 1986;27(3):225-33.

57. Ridsdale L, McKinlay A, Wojewodka G, et al. Self-management education for adults with poorly controlled epILEpsy [SMILE (UK)]: a randomised controlled trial. *Health Technol Assess*. 2018;22(21):1-142.
58. Sajatovic M, Colon-Zimmermann K, Kahriman M, et al. A 6-month prospective randomized controlled trial of remotely delivered group format epilepsy self-management versus waitlist control for high-risk people with epilepsy. *Epilepsia*. 2018;59(9):1684-1695.
59. Gillham RA. Refractory epilepsy: an evaluation of psychological methods in outpatient management. *Epilepsia*. 1990;31(4):427-32.
60. Gunter MJ, Brixner D, von Worley A, et al. Impact of a seizure disorder disease management program on patient-reported quality of life. *Dis Manag*. 2004;7(4):333-47.
61. Wiebe S, Matijevic S, Eliasziw M, et al. Clinically important change in quality of life in epilepsy. *J Neurol Neurosurg Psychiatry*. 2002;73(2):116-120.
62. Atkinson-Clark E, Charokopou M, Van Osselaer N, et al. A discrete-choice experiment to elicit preferences of patients with epilepsy for self-management programs. *Epilepsy Behav*. 2018;79:58-67.
63. Begley C, Shegog R, Harding A, et al. Longitudinal feasibility of MINDSET: a clinic decision aid for epilepsy self-management. *Epilepsy Behav*. 2015;44:143-50.
64. Johnson EK, Fraser RT, Miller JW, et al. A comparison of epilepsy self-management needs: provider and patient perspectives. *Epilepsy Behav*. 2012;25(2):150-5.
65. Laybourne AH, Morgan M, Watkins SH, et al. Self-management for people with poorly controlled epilepsy: Participants' views of the UK Self-Management in epILEpsy (SMILE) program. *Epilepsy Behav*. 2015;52(Pt A):159-64.
66. Leenen LAM, Wijnen BFM, van Haastregt JCM, et al. Process evaluation of a multi-component self-management intervention for adults with epilepsy (ZMILE study). *Epilepsy Behav*. 2017;73:64-70.
67. Ridsdale L, Philpott SJ, Krooupa AM, et al. People with epilepsy obtain added value from education in groups: results of a qualitative study. *Eur J Neurol*. 2017;24(4):609-616.
68. Snape DA, Morgan M, Ridsdale L, et al. Developing and assessing the acceptability of an epilepsy first aid training intervention for patients who visit UK emergency departments: A multi-method study of patients and professionals. *Epilepsy Behav*. 2017;68:177-185.
69. Walker ER, Bamps Y, Burdett A, et al. Social support for self-management behaviors among people with epilepsy: a content analysis of the WebEase program. *Epilepsy Behav*. 2012;23(3):285-90.
70. Leenen LAM, Wijnen BFM, de Kinderen RJA, et al. Are people with epilepsy using eHealth-tools? *Epilepsy Behav*. 2016;64(Part A):268-272.
71. Clark NM, Stoll S, Youatt EJ, et al. Fostering epilepsy self management: The perspectives of professionals. *Epilepsy Behav*. 2010;19(3):255-263.
72. Fraser RT, Johnson EK, Miller JW, et al. Managing epilepsy well: Self-management needs assessment. *Epilepsy Behav*. 2011;20(2):291-298.
73. Buelow JM. Epilepsy management issues and techniques. *J Neurosci Nurs*. 2001;33(5):260-269.
74. Begley C, Chong J, Shegog R, et al. MINDSET: Clinical feasibility of utilizing the revised epilepsy self-management tool for Spanish speaking patients. *Epilepsy Behav*. 2018;88:218-226.

75. Toivonen KI, Zernicke K, Carlson LE. Web-Based Mindfulness Interventions for People With Physical Health Conditions: Systematic Review. *J Med Internet Res*. 2017;19(8):e303.
76. Lorig KR, Holman H. Self-management education: history, definition, outcomes, and mechanisms. *Ann Behav Med*. 2003;26(1):1-7.
77. U.S. Department of Veterans Affairs. Whole Health For Life. Available at: https://www.va.gov/patientcenteredcare/. Accessed December 13, 2018.
78. U.S. Department of Veterans Affairs. Patient Care Services. Available at: https://www.patientcare.va.gov/primarycare/pact/Resources.asp. Accessed October 22, 2018.
79. Centers for Medicare and Medicaid Services. Diabetes self-management training. Available at: https://www.medicare.gov/coverage/diabetes-self-management-training. Accessed October 22, 2018.
80. Centers for Medicare and Medicaid Services. Chronic care management services. Available at: https://www.medicare.gov/coverage/chronic-care-management-services. Accessed October 22, 2018.
81. U.S. Department of Veterans Affairs. QUIET (Quality Indicators in Epilepsy Treatment) tool. Available at: https://www.epilepsy.va.gov/QUIET/index.asp. Accessed October 22, 2018.
82. Harkin B, Webb TL, Chang BP, et al. Does monitoring goal progress promote goal attainment? A meta-analysis of the experimental evidence. *Psychol Bull*. 2016;142(2):198-229.
83. Escoffery C, McGee R, Bidwell J, et al. A review of mobile apps for epilepsy self-management. *Epilepsy Behav*. 2018;81:62-69.
84. U.S. Department of Veterans Affairs. QUERI (Quality Enhancement Research Initiative. Available at: https://www.queri.research.va.gov/about/default.cfm. Accessed October 22, 2018.
85. Thompson NJ, Walker ER, Obolensky N, et al. Distance delivery of mindfulness-based cognitive therapy for depression: project UPLIFT. *Epilepsy Behav*. 2010;19(3):247-54.
86. Adam GP, Springs S, Trikalinos T, et al. Does information from ClinicalTrials.gov increase transparency and reduce bias? Results from a five-report case series. *Syst Rev*. 2018;7(1):59.

# APPENDIX A. SEARCH STRATEGIES

## PubMed: April 13, 2018 and October 31, 2018

| Set | Terms | Results |
|---|---|---|
| **#1** | "Epilepsy"[Mesh] OR epilepsy[tiab] OR epilepsies[tiab] OR epileptic[tiab] OR epileptics[tiab] OR epilepsia[tiab] | **139,312** |
| **#2** | "Self-Management"[Mesh] OR "Self Care"[Mesh] OR "Self-Control"[Mesh] OR self[tiab] OR selfcare[tiab] OR selfmanagement[tiab] OR selftreatment[tiab] OR selfcontrol[tiab] OR selfhelp[tiab] | **646,690** |
| **#3** | "Patient Compliance"[Mesh] OR "Medication Adherence"[tiab] OR "Medication Compliance"[tiab] OR "Medication nonadherence"[tiab] OR "Medication non adherence"[tiab] OR "Medication Noncompliance"[tiab] OR "Medication non compliance"[tiab] OR "Medication Persistence"[tiab] OR "Health Knowledge, Attitudes, Practice"[Mesh] | **162,567** |
| **#4** | "Behavior Therapy"[Mesh] OR behavior therap*[tiab] OR behaviour therap*[tiab] OR behavioral therap*[tiab] OR behavioural therap*[tiab] OR "anger management"[tiab] OR biofeedback[tiab] OR "bio-feedback"[tiab] OR myobiofeedback[tiab] OR myofeedback[tiab] OR "physiological feedback"[tiab] OR "neuro feedback"[tiab] OR neurofeedback[tiab] OR cognitive therap*[tiab] OR cognition therap*[tiab] OR acceptance therap*[tiab] OR commitment therap*[tiab] OR mindfulness[tiab] OR "MBSR"[tiab] OR "psychologic desensitization"[tiab] OR "psychological desensitization"[tiab] OR "Eye Movement Desensitization and Processing"[tiab] OR EMDR[tiab] OR implosive therap*[tiab] OR exposure therap*[tiab] OR relaxation therap*[tiab] OR "relaxation techniques"[tiab] OR "relaxation technique"[tiab] OR "meditation"[tiab] OR meditate[tiab] OR meditates[tiab] OR "Mind-Body Therapies"[Mesh:NoExp] OR "mind body therapy"[tiab] OR "mind body therapies"[tiab] OR "mind body medicine"[tiab] OR "Breathing Exercises"[Mesh] OR "breathing exercise"[tiab] OR "breathing exercises"[tiab] OR "respiratory muscle training"[tiab] OR "paced respiration"[tiab] OR "Imagery (Psychotherapy)"[Mesh] OR "guided imagery"[tiab] OR "Alexander Technique"[tiab] OR problem-solving therap*[tiab] OR psychodynamic therap*[tiab] OR psychotherap*[tiab] OR "stress reduced"[tiab] OR "stress reducer"[tiab] OR" stress reducers"[tiab] OR "stress reducing"[tiab] OR "stress reduction"[tiab] OR "stress reductions"[tiab] OR "stress reductive"[tiab] | **125,605** |
| **#5** | #1 AND (#2 OR #3 OR #4) AND English[lang] | **3,887** |
| **#6** | #5 NOT (animals[mh] NOT humans[mh]) NOT (("Adolescent"[Mesh] OR "Child"[Mesh] OR "Infant"[Mesh]) NOT "Adult"[Mesh]) | **3,080** |
| **#7** | #6 AND (("randomized controlled trial"[ptyp] OR "controlled clinical trial"[ptyp] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR "Comparative Study"[ptyp] OR "clinical trial"[pt] OR "clinical trial"[tiab] OR "clinical trials"[tiab] OR "evaluation studies"[ptyp] OR "evaluation studies as topic"[MeSH] OR "evaluation study"[tiab] OR "evaluation studies"[tiab] OR drug therapy[sh] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "cohort studies"[MeSH] OR cohort[tiab] OR "longitudinal studies"[MeSH] OR longitudinal[tiab] OR longitudinally[tiab] OR prospective[tiab] OR prospectively[tiab] OR "follow up"[tiab] OR "comparative study"[pt] OR "comparative studies"[tiab] OR nonrandom[tiab] OR "non-random"[tiab] OR nonrandomized[tiab] OR "non-randomized"[tiab] OR nonrandomised[tiab] OR "non-randomised"[tiab] OR quasi-experiment*[tiab] OR quasiexperiment*[tiab] OR quasirandom*[tiab] OR quasi-random*[tiab] OR quasi-control*[tiab] OR quasicontrol*[tiab] OR (controlled[tiab] AND (trial[tiab] OR study[tiab])) OR "pre-post"[tiab] OR "posttest"[tiab] OR "post-test"[tiab] OR pretest[tiab] OR pre-test[tiab] OR (before[tiab] AND after[tiab]) OR (before[tiab] AND during[tiab])) NOT (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp])) | **1,695** |

| Set | Terms | Results |
|---|---|---|
| **#8** | #6 AND (("Delivery of Health Care"[Mesh] OR "healthcare delivery"[tiab] OR "health care delivery"[tiab] OR "healthcare system"[tiab] OR "healthcare systems"[tiab] OR "health care system"[tiab] OR "health care systems"[tiab] OR "Health Facilities"[Mesh] OR outpatient[tiab] OR outpatients[tiab] OR clinic[tiab] OR clinics[tiab] OR "primary care"[tiab] OR program[tiab] OR programs[tiab] OR programme[tiab] OR programmes[tiab] OR protocol[tiab] OR protocols[tiab] OR policy[tiab] OR policies[tiab] OR guideline[tiab] OR guidelines[tiab] OR "standards"[Subheading] OR standard[tiab] OR standards[tiab] OR initiative[tiab] OR initiatives[tiab] OR strategy[tiab] OR strategies[tiab] OR "Evidence-Based Practice"[Mesh]) AND ("Program Evaluation"[Mesh] OR "Outcome and Process Assessment (Health Care)"[Mesh] OR "Diffusion of Innovation"[Mesh] OR implement[tiab] OR implements[tiab] OR implementation[tiab] OR implemented[tiab] OR implementing[tiab] OR preimplementation[tiab] OR postimplementation[tiab] OR uptake[tiab] OR adopt*[tiab] OR adapt*[tiab] OR facilitator*[tiab] OR feasible[tiab] OR feasibility[tiab] OR effective[tiab] OR effectiveness[tiab] OR barrier[tiab] OR barriers[tiab] OR benefit[tiab] OR benefits[tiab])) | **568** |
| **#9** | #7 OR #8 | **1,860** |

## Cochrane Central: April 13, 2018

| Set | Terms | Results |
|---|---|---|
| **#1** | [mh Epilepsy] OR (epilepsy or epilepsies or epileptic or epileptics or epilepsia):ti,ab,kw | **5,832** |
| **#2** | [mh "Self-Management"] OR [mh "Self Care"] OR [mh "Self-Control"] OR (self OR selfcare OR selfmanagement OR selftreatment OR selfcontrol OR selfhelp):ti,ab,kw | **62,762** |
| **#3** | [mh "Patient Compliance"] OR [mh "Health Knowledge, Attitudes, Practice"] OR ("Medication Adherence" OR "Medication Compliance" OR "Medication nonadherence" OR "Medication non adherence" OR "Medication Noncompliance" OR "Medication non compliance" OR "Medication Persistence"):ti,ab,kw | **18,270** |
| **#4** | [mh "Behavior Therapy"] OR [mh^ "Mind-Body Therapies"] OR [mh "Breathing Exercises"] OR [mh "Imagery (Psychotherapy)"] OR ((behavior near/2 therap*) or (behaviour near/2 therap*) or (behavioral near/2 therap*) or (behavioural near/2 therap*) OR "anger management" OR biofeedback OR "bio-feedback" OR myobiofeedback OR myofeedback OR "physiological feedback" OR "neuro feedback" OR neurofeedback OR (cognitive NEAR/2 therap*) OR (cognition NEAR/2 therap*) OR (acceptance NEAR/2 therap*) OR (commitment NEAR/2 therap*) OR mindfulness OR MBSR OR "psychologic desensitization" OR "psychological desensitization" OR "Eye Movement Desensitization and Processing" OR EMDR OR (implosive NEAR/2 therap*) OR (exposure NEAR/2 therap*) OR (relaxation NEAR/2 therap*) OR "relaxation techniques" OR "relaxation technique" OR meditation OR meditate OR meditates OR "mind body therapy" OR "mind body therapies" OR "mind body medicine" OR "breathing exercise" OR "breathing exercises" OR "respiratory muscle training" OR "paced respiration" OR "guided imagery" OR "Alexander Technique" OR ("problem-solving" NEAR/2 therap*) OR (psychodynamic NEAR/2 therap*) OR psychotherap* OR "stress reduced" OR "stress reducer" OR "stress reducers" OR "stress reducing" OR "stress reduction" OR "stress reductions" OR "stress reductive"):ti,ab,kw | **37,550** |
| **#5** | #1 AND (#2 OR #3 OR #4) AND English[lang] | **432** |
| **#6** | #5 NOT (([mh Adolescent] OR [mh Child] OR [mh Infant]) NOT [mh Adult]) | **326** |

## PsycINFO: April 13, 2018

| Set | Terms | Results |
|---|---|---|
| **S1** | DE "Epilepsy" OR DE "Epileptic Seizures" OR TI ( epilepsy OR epilepsies OR epileptic OR epileptics OR epilepsia) OR AB ( epilepsy OR epilepsies OR epileptic OR epileptics OR epilepsia) | **38,409** |
| **S2** | DE "Self-Management" OR DE "Self-Monitoring" OR DE "Self-Control" OR TI ( self OR selfcare OR selfmanagement OR selftreatment OR selfcontrol OR selfhelp) OR AB ( "self-care*" OR "self-manage*" OR "self-treat*" OR "self-control" OR "self-help" OR "self care" OR "self management" OR "self treatment" OR "self control" OR "self help" OR selfcare OR selfmanagement OR selftreatment OR selfcontrol OR selfhelp) | **160,644** |
| **S3** | DE "Compliance" OR DE "Treatment Compliance" OR DE "Health Attitudes" OR TI ( "Medication Adherence" OR "Medication Compliance" OR "Medication nonadherence" OR "Medication non adherence" OR "Medication Noncompliance" OR "Medication non compliance" OR "Medication Persistence") OR AB ( "Medication Adherence" OR "Medication Compliance" OR "Medication nonadherence" OR "Medication non adherence" OR "Medication Noncompliance" OR "Medication non compliance" OR "Medication Persistence") | **29,260** |
| **S4** | DE "Behavior Therapy" OR DE "Guided Imagery" OR DE "Alternative Medicine" OR DE "Stress and Coping Measures" OR DE "Stress Management" OR DE "Emotional Control" OR DE "Anger Control" OR DE "Relaxation Therapy" OR DE "Progressive Relaxation Therapy" OR DE "Mindfulness" OR AB ( "behavior therap*" OR "behaviour therap*" OR "behavioral therap*" OR "behavioural therap*" OR "anger management" OR biofeedback OR "bio-feedback" OR myobiofeedback OR myofeedback OR "physiological feedback" OR "neuro feedback" OR neurofeedback OR "cognitive therap*" OR "cognition therap*" OR "acceptance therap*" OR "commitment therap*" OR mindfulness OR "MBSR" OR "psychologic desensitization" OR "psychological desensitization" OR "Eye Movement Desensitization and Processing" OR EMDR OR "implosive therap*" OR "exposure therap*" OR "relaxation therap*" OR "relaxation techniques" OR "relaxation technique" OR meditation OR meditate OR meditates OR "mind body therapy" OR "mind body therapies" OR "mind body medicine" OR "breathing exercise" OR "breathing exercises" OR "respiratory muscle training" OR "paced respiration" OR "guided imagery" OR "Alexander Technique" OR "problem-solving therap*" OR "psychodynamic therap*" OR psychotherap* OR "stress reduced" OR "stress reducer" OR "stress reducers" OR "stress reducing" OR "stress reduction" OR "stress reductions" OR "stress reductive" ) OR TI ( "behavior therap*" OR "behaviour therap*" OR "behavioral therap*" OR "behavioural therap*" OR "anger management" OR biofeedback OR "bio-feedback" OR myobiofeedback OR myofeedback OR "physiological feedback" OR "neuro feedback" OR neurofeedback OR "cognitive therap*" OR "cognition therap*" OR "acceptance therap*" OR "commitment therap*" OR mindfulness OR MBSR OR "psychologic desensitization" OR "psychological desensitization" OR "Eye Movement Desensitization and Processing" OR EMDR OR "implosive therap*" OR "exposure therap*" OR "relaxation therap*" OR "relaxation techniques" OR "relaxation technique" OR meditation OR meditate OR meditates OR "mind body therapy" OR "mind body therapies" OR "mind body medicine" OR "breathing exercise" OR "breathing exercises" OR "respiratory muscle training" OR "paced respiration" OR "guided imagery" OR "Alexander Technique" OR "problem-solving therap*" OR "psychodynamic therap*" OR psychotherap* OR "stress reduced" OR "stress reducer" OR "stress reducers" OR "stress reducing" OR "stress reduction" OR "stress reductions" OR "stress reductive" ) | **183,898** |
| **S5** | S1 AND (S2 OR S3 OR S4) Limiters - Publication Type: All Journals; Language: English; Age Groups: Adulthood (18 yrs & older); Population Group: Human; Document Type: Journal Article; Exclude Dissertations | **583** |

## CINAHL: April 13, 2018

| Set | Terms | Results |
|---|---|---|
| **S1** | (MH "Epilepsy+") OR TI ( epilepsy OR epilepsies OR epileptic OR epileptics OR epilepsia) OR AB ( epilepsy OR epilepsies OR epileptic OR epileptics OR epilepsia) | **18,173** |
| **S2** | (MH "Self Care+") OR TI ( self OR selfcare OR selfmanagement OR selftreatment OR selfcontrol OR selfhelp) OR AB ( "self-care*" OR "self-manage*" OR "self-treat*" OR "self-control" OR "self-help" OR "self care" OR "self management" OR "self treatment" OR "self control" OR "self help" OR selfcare OR selfmanagement OR selftreatment OR selfcontrol OR selfhelp) | **97,606** |
| **S3** | (MH "Patient Compliance+") OR (MH "Attitude to Health+") OR TI ( "Medication Adherence" OR "Medication Compliance" OR "Medication nonadherence" OR "Medication non adherence" OR "Medication Noncompliance" OR "Medication non compliance" OR "Medication Persistence") OR AB ( "Medication Adherence" OR "Medication Compliance" OR "Medication nonadherence" OR "Medication non adherence" OR "Medication Noncompliance" OR "Medication non compliance" OR "Medication Persistence") | **129,591** |
| **S4** | (MH "Behavior Modification+") OR (MH "Guided Imagery") OR (MH "Control (Psychology)+") OR (MH "Biofeedback") OR AB ( "behavior therap*" OR "behaviour therap*" OR "behavioral therap*" OR "behavioural therap*" OR "anger management" OR biofeedback OR "bio-feedback" OR myobiofeedback OR myofeedback OR "physiological feedback" OR "neuro feedback" OR neurofeedback OR "cognitive therap*" OR "cognition therap*" OR "acceptance therap*" OR "commitment therap*" OR mindfulness OR "MBSR" OR "psychologic desensitization" OR "psychological desensitization" OR "Eye Movement Desensitization and Processing" OR EMDR OR "implosive therap*" OR "exposure therap*" OR "relaxation therap*" OR "relaxation techniques" OR "relaxation technique" OR meditation OR meditate OR meditates OR "mind body therapy" OR "mind body therapies" OR "mind body medicine" OR "breathing exercise" OR "breathing exercises" OR "respiratory muscle training" OR "paced respiration" OR "guided imagery" OR "Alexander Technique" OR "problem-solving therap*" OR "psychodynamic therap*" OR psychotherap* OR "stress reduced" OR "stress reducer" OR "stress reducers" OR "stress reducing" OR "stress reduction" OR "stress reductions" OR "stress reductive" ) OR TI ( "behavior therap*" OR "behaviour therap*" OR "behavioral therap*" OR "behavioural therap*" OR "anger management" OR biofeedback OR "bio-feedback" OR myobiofeedback OR myofeedback OR "physiological feedback" OR "neuro feedback" OR neurofeedback OR "cognitive therap*" OR "cognition therap*" OR "acceptance therap*" OR "commitment therap*" OR mindfulness OR MBSR OR "psychologic desensitization" OR "psychological desensitization" OR "Eye Movement Desensitization and Processing" OR EMDR OR "implosive therap*" OR "exposure therap*" OR "relaxation therap*" OR "relaxation techniques" OR "relaxation technique" OR meditation OR meditate OR meditates OR "mind body therapy" OR "mind body therapies" OR "mind body medicine" OR "breathing exercise" OR "breathing exercises" OR "respiratory muscle training" OR "paced respiration" OR "guided imagery" OR "Alexander Technique" OR "problem-solving therap*" OR "psychodynamic therap*" OR psychotherap* OR "stress reduced" OR "stress reducer" OR "stress reducers" OR "stress reducing" OR "stress reduction" OR "stress reductions" OR "stress reductive" ) | **71,641** |
| **S5** | S1 AND (S2 OR S3 OR S4) Limiters - English Language; Age Groups: All Adult; Publication Type: Journal Article | **238** |

**Searches retrieved 2,996 records before duplicates were removed.**

# APPENDIX B. PEER REVIEW COMMENTS/AUTHOR RESPONSES

| Question Text | Reviewer Number | Comment | Response |
|---|---|---|---|
| Are the objectives, scope, and methods for this review clearly described? | 1 | Yes | Acknowledged |
| | 2 | Yes | Acknowledged |
| | 3 | Yes | Acknowledged |
| | 4 | Yes | Acknowledged |
| | 6 | Yes | Acknowledged |
| | 7 | Yes | Acknowledged |
| Is there any indication of bias in our synthesis of the evidence? | 1 | No | Acknowledged |
| | 2 | No | Acknowledged |
| | 3 | No | Acknowledged |
| | 4 | No | Acknowledged |
| | 6 | No | Acknowledged |
| | 7 | No | Acknowledged |
| Are there any published or unpublished studies that we may have overlooked? | 1 | No | Acknowledged |
| | 2 | No | Acknowledged |
| | 3 | Yes - Would consider an addendum to include the Sajatovic et al study in Epilepsia Sept 2018, 1684-95. This study appears to have a positive outcome and may offset some to the disappointment of the other negative or inconclusive studies reviewed. | Thank you. We identified this study when we updated our search and it is included in the final report. |
| | 4 | No | Acknowledged |
| | 6 | Yes - Sajatovic M et al. A 6-month prospective randomized controlled trial of remotely delivered group format epilepsy self-management versus waitlist control for high-risk people with epilepsy. Epilepsia. 2018;59 (9):1684–1695) | Thank you. We identified this study when we updated our search and it is included in the final report. |
| | 7 | There are a number of published studies that would make the case for why this is important based on data for Veterans. | We cite Veteran-specific data obtained from the Epilepsy Centers of Excellence. |
| Additional suggestions or comments can be provided below. If applicable, | 1 | Recommend clearly defining "self-efficacy" and how this differs from self-management.<br>On page 3 (and elsewhere) it is stated that 6 educational interventions and 8 psychosocial therapy interventions were included for review in KQ1; however, the Table lists these numbers as 6 and 12 respectively. Please clarify the reason for this difference. | Self-management is carefully defined in the report. We have added a definition for self-efficacy.<br>This apparent discrepancy relates to the number of studies using the interventions versus the number of intervention arms using the |

| Question Text | Reviewer Number | Comment | Response |
|---|---|---|---|
| please indicate the page and line numbers from the draft report. | | | interventions. We have carefully edited to specify studies or intervention arms. |
| | 2 | Document is quite thorough, well-written and clear. Though it does not directly address patient centered care or Whole Health, findings regarding the importance of personalization for implementation are relevant.<br>Pg. 50, lines 9-11; Suggested rewording: Self-management of chronic illness that is aligned with an individual's values and preferences is considered an important component in delivering patient-centered care in VHA, and is a pillar of VHA's Patient Aligned Care Teams (PACT).<br>I am unfamiliar with the reference cited (#75) and am not sure that it is reflective of current perspectives re. Whole Health and PCC in VHA. The Office of Patient Centered Care and Cultural Transformation website is: https://vaww.va.gov/patientcenteredcare/ | Thank you. The suggested edit has been made.<br>We think the reference is relevant. We have added a link to the Office of Patient Centered Care and Cultural Transformation. |
| | 3 | Reference 2 is not sited properly (ref 2 on page 9 does not seem to match ref 2 on page 48).<br>Could not find a definition regarding how a setting was deemed eligible. | Thank you for detecting this citation error. The citation has been updated (Rehman et al., 2015).<br>Setting is described in Table 1 (Eligibility Criteria). “Setting” is this instance refers to eligible modes of delivery, rather than a physical location. |
| | 4 | | |
| | 6 | It is well written and valuable to providers in VAH.<br>I found following descriptions that may be revised if the most recent publication (see below) will be included.<br>Page 8 (p 2) Data Sources and Searches<br>We searched MEDLINE (via PubMed), PsycINFO, and CINAHL from inception through April 13, 2018. We also examined the bibliographies of recent reviews for additional relevant studies. | Thank you.<br>Thank you. Except as noted, these statements were revised after the addition of the Sajatovic study.<br>This statement is accurate. |

| Question Text | Reviewer Number | Comment | Response |
|---|---|---|---|
| | | Page 12 (p 6) “No studies directly addressed facilitators and barriers to implementing and adopting self-management interventions for patients with epilepsy in the VHA or other large health systems. No studies directly enrolled Veterans with epilepsy.”<br>Page 12 (p6) “We found limited evidence for benefit on selected primary or secondary outcomes.<br>Educational self-management interventions may improve the use of self-management practices.<br>Sparse evidence suggested possible benefit of psychosocial therapy interventions on self efficacy.<br>Self-management interventions did not improve other outcomes but the certainty of evidence for these finding was often low.” | These statements about educational interventions were updated. |
| | | Page 13 (p7) “None of the included studies were conducted in VHA or specifically with Veterans.”<br>Page 13 (p7) Conclusions “These self-management interventions showed clinically important benefit for only a limited number of outcomes, but the confidence in these findings was mostly low.” | This statement remains accurate. |
| | | There is a recent article published in Epilepsia September issue of 2018 (Sajatovic M, Colon-Zimmermann K, Kahriman M, Fuentes-Casiano E, Liu H, Tatsuoka C, Cassidy KA, Lhatoo S, Einstadter D, Chen P. A 6-month prospective randomized controlled trial of remotely delivered group format epilepsy self-management versus waitlist control for high-risk people with epilepsy. Epilepsia. 2018;59 (9):1684–1695)<br>This study, if included in this review, will enhance the quality of current review and alter narratives described above in executive summary and through the rest of manuscript of review.<br>This study was conducted at the Cleveland VA Medical Center, and University Hospitals of Cleveland Neurological Institute, with subjects including veterans. I would recommend to include this study in this review. It is a randomized controlled trial using remotely delivered group format epilepsy self-management (n=60) versus waitlist control (n=6) for | This study is included in the final report. |

| Question Text | Reviewer Number | Comment | Response |
|---|---|---|---|
| | | high risk individuals with epilepsy. This study will help in addressing all 3 questions this review intended to answer, and will enhance the quality of this review.<br>Summary of this study is as below.<br>Objective: Despite advances in care, many people with epilepsy have negative health events (NHEs) such as accidents, emergency department visits, and poor quality of life. Self-management for people with epilepsy and a history of negative health events"(SMART) is a novel group format epilepsy self-management intervention. A community participatory approach informed the refinement of SMART, which was then tested in a 6-month randomized controlled trial of SMART (n = 60) versus waitlist control (WL, n = 60).<br>Methods: Participants were adults aged ≥18 years with epilepsy and an NHE within the past 6 months (seizure, accident, self-harm attempt, emergency department visit, or hospitalization). Assessments were conducted at screening, baseline, 10 weeks, and 24 weeks (6 months). Primary outcome was 6-month change in total NHE count. Additional outcomes included depression on the nine-item Patient Health Questionnaire and Montgomery-Asberg Depression Rating Scale, quality of life on the 10-item Quality of Life in Epilepsy, functioning on the 36-item Short-Form Health Survey, and seizure severity on the Liverpool Seizure Severity Scale.<br>Results: Mean age was 41.3 years (SD = 11.82), 69.9% were African American, 74.2% were unemployed, and 87.4% had an annual income < US$25 000; 57.5% had a seizure within 30 days of enrollment. Most NHEs were seizures. Six-month study attrition was 14.2% overall and similar between arms. Individuals randomized to SMART had greater reduction in total median NHEs from baseline to 6 months compared to WL (P = 0.04). SMART was also associated with improved nine-item Patient Health Questionnaire (P = 0.032), Montgomery-Asberg Depression Rating Scale (P = 0.002), 10-item Quality of Life in Epilepsy (P < 0.001), and 36-item Short-Form Health Survey (P = 0.015 physical health, P = 0.003 mental health) versus WL. There was no difference in seizure severity. | |

| Question Text | Reviewer Number | Comment | Response |
|---|---|---|---|
| | | Significance: SMART is associated with reduced health complications and improved mood, quality of life, and health functioning in high-risk people with epilepsy. Additional efforts are needed to investigate potential for scale-up.<br>Curriculum of “Self-management for people with epilepsy and a history of negative health events” (SMART)<br>Session 1 Orientation and introductions; Emphasize ground rules; Establishment of a therapeutic relationship; Facts and myths about epilepsy and general epilepsy management principles<br>Session 2 Relationship of epilepsy and stress; Stigma and “double stigma”; Strategies to cope with stigma; Introduction to personal goal-setting<br>Session 3 Treatments for epilepsy; Complications of epilepsy; Minimizing epilepsy complications; The importance of daily routine and good sleep habits<br>Session 4 Problem-solving skills and the IDEA approach (Identify the problem, Define possible solutions, Evaluate the solutions, Act on the best solution); Talking with your health care providers; Role play of communication with care providers<br>Session 5 Nutrition for best physical and emotional health; Substance abuse and its effects on epilepsy; Specific stress-management approaches<br>Session 6 Effects of exercise and being outdoors on physical and emotional health; Medication routines; Prioritizing medication side effects and discussing it with your clinician<br>Session 7 Social supports and using your available supports; Advocacy groups for epilepsy; A personal care plan to take care of the mind and the body<br>Session 8 Normalizing your life in spite of having a chronic but unpredictable condition; Self- management as a life-style; Acknowledgement of group progress; Setting the stage for Ongoing Illness Management and Recovery (Step 2) | |
| | 7 | The references in the body of the document seemed to be the wrong references. | Thank you, the references have been updated. |

# APPENDIX C. INTERVENTION CHARACTERISTICS TABLES

For full study citations in this appendix, please refer to the report's main reference list.

## RANDOMIZED TRIALS

| Study | Setting/Delivery Mode<br>Intervention Target | Type of Provider<br>Specialized Training | Intervention Skills | Intervention Techniques<br>Goal-setting | Frequency/ Duration of Contact<br>Comparator |
|---|---|---|---|---|---|
| ***Educational Self-management Interventions*** | | | | | |
| DiIorio, 2011[47] | Asynchronous internet-based delivery[a]<br>Patient targeted | Peer online discussion forum, electronic-based delivery<br>No special training | · Knowledge<br>· Symptom-monitoring using MyLog<br>· Problem-solving, decision-making: "planning the next steps"<br>· Stress management module<br>· Sleep module<br>· Medication adherence module | CBT, PST, relaxation technique, sleep intervention, motivational interviewing<br>Collaborative goal-setting and automated goal-setting | Weekly use of program for 6 weeks; length of sessions not specified<br>Waitlist control |
| Fraser, 2015[48] | · Group-based intervention, with 1 peer with epilepsy as the leader[a]<br>· Additional written information via workbook and mailed materials<br>Patient targeted | · Peer with epilepsy, 7 years' experience as a neurologic employment specialist<br>· Social worker-delivered: rehabilitation psychologist<br>No special training | · Explicit knowledge<br>· Problem-solving, decision-making: assertive communication, "managing my epilepsy" care module<br>· Stress management: dealing with stress and the blues modules<br>· Mailed materials on "safe exercise programs" as related to individuals' goals | · Likely CBT-based, but not explicitly stated<br>· Multicomponent intervention with CBT-related skills of problem solving and stress management<br>Collaboratively set weekly personal goals | 8 weekly, 75-minute sessions<br>Waitlist control |

| Study | Setting/Delivery Mode Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques Goal-setting | Frequency/ Duration of Contact Comparator |
|---|---|---|---|---|---|
| | | | · Medication adherence: “managing my epilepsy” care module | | |
| Helgeson,1990[51] | Large group-based intervention with multimedia presentation[a]<br>Patient targeted, but family invited to attend | Not reported | · Explicit knowledge<br>· Problem-solving, decision-making skills to identify and cope with psychological, social, family, and work-related problems<br>· Information on compliance issues related to epilepsy | Identification and coping skills presented as “cognitive-behavioral”<br>Goal-setting not presented | 2 consecutive days<br>Waitlist control |
| May, 2002[53] | · Group-based intervention with 2 instructors[a]<br>· Written manual also provided<br>Patient targeted | Any professionals or peers are eligible, but not reported for current study<br>MOSES training required | · Explicit knowledge<br>· Discussion of how to self-monitor and record symptoms<br>· Discussion of problem-solving for seizure risk factors<br>· Discussion of gaining emotional-coping skills<br>· Discussion of communication and cooperation with provider, including medication management | · Explicit education and didactic discussions<br>· Multicomponent intervention with CBT-related and PST-related skills of problem-solving and stress management<br>· CBT and PST not explicitly discussed<br>Goal-setting not presented | 2 consecutive days totaling 16 hours<br>Waitlist control |

| Study | Setting/Delivery Mode Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques Goal-setting | Frequency/ Duration of Contact Comparator |
|---|---|---|---|---|---|
| Ridsdale, 2018[57] | Group-based intervention with 2 trained epilepsy nurse specialists<br>Patient targeted, but family invited to attend | Epilepsy nurse specialists and clinical psychologists trained in SMILE<br>SMILE specialized training required | · Explicit knowledge<br>· Discussion of how to self-monitor and record symptoms<br>· Discussion of problem-solving for seizure risk factors<br>· Discussion for gaining self-efficacy of seizure control<br>· Discussion of stress management<br>· Discussion of safety, including preventing injuries | · Explicit education and didactic discussions<br>· Multicomponent intervention with CBT-related and PST-related skills of problem-solving and stress management<br>· CBT and PST never explicitly discussed<br>Goal-setting not presented | 2 consecutive days totaling 16 hours<br>Waitlist control |

| Study | Setting/Delivery Mode Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques Goal-setting | Frequency/ Duration of Contact Comparator |
|---|---|---|---|---|---|
| Sajatovic 2018[58] | · Group-based intervention with in-person, followed by synchronous internet-based delivery led by 1 trained nurse educator and 1 trained peer educator.<br>· Follow-up 1:1 telephone calls with nurse educator and peer educator<br>Patient targeted | 2-person interventionist team of one nurse educator and one peer educator<br>2-day specialized training and ongoing check-in support | · Explicit knowledge<br>· Discussion of problem-solving techniques using "IDEA" framework<br>· Discussion of stress management strategies<br>· Discussion of physical activity, sleep, and decreased substance abuse benefits<br>· Discussion of diet benefits<br>· Discussion and role-playing of communication with providers<br>· Discussion of medication adherence and side-effects management | · Explicit education and didactic discussions<br>· Problem-solving technique practice via "IDEA" framework<br>· Role-playing communication with providers<br>Patient-driven goal setting and checking on goal progress | Roughly 8 weeks of group sessions, where the first in-person session was 60-90 minutes, followed by 6 phone calls over 12 weeks of 10-15 minutes each<br>Waitlist control |
| ***Psychosocial Therapy Self-management Interventions*** | | | | | |
| Caller, 2016[46]<br>Arm 1=PST | · In-person group orientation<br>· Telephonic individual sessions, with memory coach[a]<br>· Written educational materials<br>Patient targeted | Epilepsy specialized nurse (RN or ARNP)<br>No training required | · Explicit knowledge<br>· Problem-solving therapy for organizational skills, seizure management, and social skills | · Explicit education<br>· Problem-solving therapy<br>Collaborative goal-setting | Eight 45-60 minute sessions<br>Active comparator and waitlist control |
| Caller, 2016[46]<br>Arm 2=PST plus | · In-person group orientation | Epilepsy specialized nurse (RN or ARNP) | · Explicit knowledge<br>· Problem-solving therapy for | · Explicit education<br>· Problem-solving therapy | · Eight 45-60 minute sessions |

| Study | Setting/Delivery Mode Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques Goal-setting | Frequency/ Duration of Contact Comparator |
|---|---|---|---|---|---|
| | · Telephonic individual sessions, with memory coach[a]<br>· Asynchronous training on commercial gaming device[a]<br>· Written educational materials<br><br>Patient targeted | No training required | organizational skills, seizure management, and social skills<br>· Cognitive training with gaming console | · Cognitive training via gaming console<br><br>Collaborative goal-setting | · 8 weeks of 20-40 minutes of training on gaming console 5 times/week (40 sessions)<br><br>Active comparator and waitlist control |
| Gandy, 2014[49] | · In-person introductory sessions<br>· Individual in-person sessions[a]<br><br>Patient targeted | · Predoctoral clinical psychology interns<br>· One-day treatment manual training | · Explicit knowledge:<br>· Symptom management<br>· Problem-solving skills<br>· Communication training<br>· Coping with anxiety and depression related to epilepsy<br>· Medication adherence | · Explicit education and didactic discussions<br>· Multicomponent CBT<br>· Behavioral activation<br>· Symptom-monitoring<br><br>Collaborative goal-setting | · 1-2 hour introductory session<br>· 8 weeks for 60 minutes each<br><br>Waitlist control |
| Haut, 2018[50] | · In-person training session and refresher session<br>· Smartphone-assisted asynchronous 2-3 times daily communication<br><br>Patient targeted | Psychologist<br><br>No training specified | · Implicit knowledge<br>· Symptom/seizure tracking with e-diary<br>· Relaxation training via PMR | · PMR<br>· Symptom/seizure monitoring<br><br>Goal-setting not presented | · Two 1-hour training sessions<br>· 12 weeks of twice daily PMR for a total of 20 minutes/day<br>· 3 times/day e-diary reporting |

| Study | Setting/Delivery Mode Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques Goal-setting | Frequency/ Duration of Contact Comparator |
|---|---|---|---|---|---|
| | | | | | · Additional e-diary reporting based on seizure events<br>Active focused-attention |
| Leenen, 2018[52] | · In-person group sessions led by 2 nurse-practitioners[a]<br>· Smartphone-assisted tracking via Eppy app<br>· MEMS Caps<br>Patient targeted but family invited to attend | Nurse practitioners<br>No training specified | · Explicit knowledge<br>· Symptom/seizure tracking<br>· Stress management via proactive coping<br>· Evaluation and management of risks<br>· Medication management<br>· Decision-making and communication with providers | · Explicit education and didactic discussions<br>· Symptom/seizure monitoring<br>· Proactive coping with stressors training<br>· Medication management and monitoring<br>Collaborative goal-setting | · 5 weekly 2-hour sessions and one 2-hour booster<br>· Eppy app tracking, time not reported<br>Treatment as usual |
| McLaughlin, 2011[54]<br>Arm 1=CBT | · In-person group sessions led by a psychologist[a]<br>· Daily seizure diary<br>Patient targeted | Psychologist<br>Expertise in CBT for epilepsy | · Explicit knowledge<br>· Symptom/seizure tracking<br>· Symptoms and triggers identification<br>· Stress management via cognitive restructuring<br>· Information on diet, physical activity, sleep, and substances<br>· Information on utilizing social supports | · Explicit education and didactic discussions<br>· Multicomponent group CBT<br>· Symptom/seizure tracking<br>· Medication management and monitoring<br>Goal-setting not presented | Six 2-hour weekly sessions<br>Active relaxation |

| Study | Setting/Delivery Mode Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques Goal-setting | Frequency/ Duration of Contact Comparator |
|---|---|---|---|---|---|
| | | | · Medication management | | |
| McLaughlin, 2011[54]<br>Arm 2=Relaxation | · In-person group sessions, led by a psychologist[a]<br>· Audiotapes of relaxation exercises<br>· Daily seizure diary<br>Patient targeted | Psychologist<br>No training specified | · Explicit knowledge<br>· Symptom/seizure tracking<br>· Relaxation training | · Explicit education and didactic discussions<br>· Relaxation training (reported as not PMR but appears to be PMR)<br>· Symptom/seizure tracking<br>Goal-setting not presented | · Six 1-hour weekly sessions<br>· Audiotapes with no time specified<br>Active relaxation |
| Puskarich, 1992[55] | · In-person sessions (unclear if group or individual)[a]<br>· Assigned at-home relaxation practice<br>Patient targeted | Not reported | · Implicit knowledge<br>· Relaxation training via PMR | PMR<br>Prescribed goal-setting | · 6 sessions (first=60 minutes, second and third=50 minutes, fourth=40 minutes, fifth=20 minutes, sixth=15 minutes)<br>· At-home practice 2 times/day for 20 minutes each for 3 weeks<br>Inactive control: quiet sitting |

| Study | Setting/Delivery Mode Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques Goal-setting | Frequency/ Duration of Contact Comparator |
|---|---|---|---|---|---|
| Tan, 1986[56] | · In-person group sessions[a]<br>· Educational materials provided<br><br>Patient targeted | "Therapist"; otherwise not reported | · Explicit knowledge<br>· Symptom/seizure tracking<br>· Tracking of stress triggers, including events, thoughts, feelings<br>· Stress management via stress inoculation and coping skills<br>· Relaxation<br>· Problem-solving skills, including vocational problems<br>· Increasing social skills and assertive communication | · Multicomponent CBT<br>· Hierarchical exposures (stress inoculation)<br>· Symptom/seizure tracking<br><br>Collaborative goal-setting | 8 weekly 2-hour sessions<br><br>Active supportive counseling and waitlist control |

[a] Primary target of the intervention.

Abbreviations: ARNP=advanced registered nurse practitioner; CBT=cognitive behavioral therapy; MEM=Medication Event Monitoring System; MOSES=Modular Service Package Epilepsy; NP=nurse practitioner; PMR=progressive muscle relaxation; PST=problem-solving therapy; SMILE=Stress Management Intervention for Living with Epilepsy; RN=registered nurse

## NONRANDOMIZED TRIALS

| Study | Setting/Delivery Mode Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques Goal-setting | Frequency/ Duration of Contact Comparator |
|---|---|---|---|---|---|
| ***Educational Self-management Interventions*** | | | | | |
| Gunter, 2004[60] | · Education workbook[a]<br>· In-person educational class, led by neurology nurse practitioner | Neurology nurse practitioner | · Explicit knowledge<br>· Symptom/seizure tracking | · Explicit education and didactic discussions<br>· Symptom/seizure tracking | Optional monthly 1-hour group education; maximum study duration 3 years and 5 months |

| Study | Setting/Delivery Mode<br>Intervention Target | Type of Provider Specialized Training | Intervention Skills | Intervention Techniques<br>Goal-setting | Frequency/ Duration of Contact<br>Comparator |
|---|---|---|---|---|---|
| | · Seizure diary<br>· Patient ID card with condition information<br>· Resource list from Epilepsy Foundation of America<br>Patient targeted | No training specified | | Goal-setting not presented | Inactive treatment as usual at 3 nonrandomly selected control sites |
| ***Psychosocial Therapy Self-management Interventions*** | | | | | |
| Gillham,1990 [59]<br>Arm 1=Self-control of seizure treatment only | In-person individual sessions[a]<br>Patient targeted | Not reported | · Explicit knowledge<br>· Symptom/seizure tracking<br>· Relaxation via deep breathing<br>· Provocation avoidance training | · Explicit education and didactic discussions<br>· Relaxation training (deep breathing)<br>Goal-setting not presented | Initial 2-hour session, followed by two 1-hour sessions for self-control of seizure treatment |
| Gillham,1990 [59]<br>Arms 2 and 3= Psychological treatment and self-control treatment | In-person individual sessions[a]<br>Patient targeted; relatives involved in identifying psychiatric/social issues, but not clear that they were targeted for treatment | Not reported | · Explicit knowledge<br>· Stress management for various comorbid psychological problems (*eg*, anxiety, mild depression, family issues)<br>· Symptom/seizure tracking<br>· Relaxation via deep breathing<br>· Provocation avoidance training | · Explicit education and didactic discussions<br>· Brief psychological intervention (likely CBT-based, but not explicitly stated<br>· Relaxation training (deep breathing)<br>Goal-setting not presented | · Initial 2-hour session followed by two 1-hour sessions for psychological problems<br>· Followed by initial 2-hour session followed by two 1-hour sessions for self-control of seizure treatment<br>· Order of treatment targets was balanced across 2 different treatment arms |

[a] Primary target of the intervention.

Abbreviation: CBT=cognitive behavioral therapy

# APPENDIX D. STUDY CHARACTERISTICS TABLE

For full study citations in this appendix, please refer to the report's main reference list.

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| Caller, 2016[46]<br>USA<br>66<br>3 | Inclusion: Patients age 18-65 with epilepsy (controlled or uncontrolled) and with subjective memory complaints<br><br>Exclusion: Severe mental impairment or IQ <70, visual impairment that precluded reading or writing, no reliable phone access | No acronym<br><br>Multidimensional psychoeducational and problem-solving intervention for cognitive difficulties through in-person group orientation and telephonic individual sessions with a trained memory coach. One of 3 arms delivered PST and working memory training on a gaming device<br><br>Comparators: PST+ cognitive training vs PST only vs treatment as usual | 45.8 (SD 9.9)<br><br>70% female<br><br>Race: NR<br><br>Marital status: NR | 38% employed<br><br>Generalized: 9<br><br>Time since diagnosis: NR<br><br>59% with seizure in the last month | Depressive symptoms<br>QOL: QOLIE-31<br><br>Primary outcome: QOLIE-31<br><br>Timing: 8 weeks | Objective: High<br><br>Patient-reported: High |
| DiIorio, 2011[47]<br>USA<br>194<br>2 | Inclusion: Adult patients with epilepsy; have taken AEDs for at least 3 months; can read and speak English; have internet access with no prior experience with WebEase | WebEase (Epilepsy Awareness, Support, and Education) study<br><br>Web program tailored to patient's stage of change; each module patients asked to assess current status, reflect on current behaviors, decide if change is needed, | 40.9 (SD 13.27)<br><br>74% female<br><br>84.3% white<br><br>48% married | 50% employed<br><br>Focal: 60<br>Generalized: 76<br>Unknown seizure: 6<br><br>Time since diagnosis: NR | Distress symptoms<br>QOL: QOLIE-10<br>Disease knowledge<br>Medication adherence: MAS<br>Self-efficacy: ESES<br>Self-management: ESMS | Objective: NA<br><br>Patient-reported: High |

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| | | and make a goal/action plan to change<br>Comparator: waitlist control | | Mean seizure frequency: 10.0 in past 30 days (SD 29.42) | Primary outcome: NR<br>Timing: Baseline, 6 weeks,12 weeks | |
| Fraser, 2015[48]<br>USA<br>92<br>2 | Inclusion: Age ≥18, with epilepsy for ≥6 months and MOCA >21; fluent in English<br>Exclusion: Active serious mental illness; IQ <70 or known cognitive impairment (MOCA ≤21) | PACES (Program for Active Consumer Engagement in Self-management)<br>Group-based psychoeducational intervention based specifically on an initial consumer survey with sessions led by an epilepsy professional and a peer with epilepsy; participants were mailed informational material related to their specific goals each week and were given a workbook with written materials<br>Comparator: treatment as usual | 45.2 (SD 12.5)<br>55% female<br>Race:<br>81% white<br>36% married | 41% employed<br>Focal: 58<br>Generalized: 44<br>Unknown seizure: 4<br>Time since diagnosis: NR<br>Median seizure frequency: 1 (IQR 1.2) | Anxiety symptoms<br>Depressive symptoms<br>QOL: QOLIE-31<br>Self-efficacy: ESES<br>Self-management: ESMS<br>Primary outcome: NR<br>Timing: Baseline, 8 weeks, 6 months | Objective: NA<br>Patient-reported: Unclear |
| Gandy, 2014[49]<br>Australia<br>59<br>2 | Inclusion: Adults (18-65) with formal diagnosis of epilepsy confirmed by treating neurologist; at least low average intelligence | CBT (Cognitive Behavior Therapy to Improve Mood in People with Epilepsy)<br>Included CBT and self-management of epilepsy: psychoeducation, managing triggers, enhancing problem | 39.3 (SD 12.57)<br>64% female<br>Race: NR<br>60% married, cohabiting | 64% employed<br>Focal: 35<br>Generalized: 10<br>Mean time since diagnosis: 13.3 years (SD 10.95) | Anxiety symptoms<br>Depressive symptoms<br>QOL: QOLIE-31 | Objective: NA<br>Patient-reported: High |

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| | Exclusion: Psychotic disorder; acutely suicidal; severe personality disorder; about to undergo epilepsy surgery | solving, managing medication adherence; delivered by trained psychology doctoral-level interns<br>Comparator: waitlist | 40% divorced, widowed, single | Seizure frequency: NR | Primary outcome: Depressive symptoms<br>Timing: Pretreatment, 2 months; post-treatment, 3 months | |
| Gillham,1990[59]<br>Europe<br>59<br>3 | Inclusion: Clinical diagnosis of epilepsy; rated by self and clinician as inadequately controlled; averaged ≥2 seizures per week in the previous 2 months with no trend toward improvement | No acronym<br>Self-control: identification of seizure semiology, training in identification of seizure symptoms, training in avoidance of provocations, relaxation techniques during prodrome, general relaxation/breathing techniques<br>Psychological intervention: targeted problems, most commonly phobic avoidance, mild depression, and family relationships<br>Comparator: Self-control vs self-control followed by psychological intervention vs psychological intervention followed by self-control | 31.7 (SD 12.1)<br>58% female<br>Race: NR<br>41% married | Employment: NR<br>Focal: 26<br>Generalized: 29<br>Unknown seizure: 4<br>Mean tine since diagnosis: 17.9 years (SD 11.7)<br>Seizure frequency: NR | Anxiety symptoms<br>Depressive symptoms<br>Seizure rate<br>Primary outcome: Seizure rate<br>Timing: Baseline, 42 weeks | Objective: NA<br>Patient-reported: High |

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| Gunter, 2004[60]<br>USA<br>747<br>2 | Inclusion: Electronic medical record identification of potential candidates, followed by physician verification of presence of epilepsy<br>Exclusion: Those identified as "do not contact" by primary care physicians (presumed these were individuals identified as not having epilepsy) | Seizure Disorder Episodes of Care (no acronym)<br>The intervention consisted of both physician resources and direct-to-patient resources; patient resources included an education workbook, a monthly hour-long seizure education class led by a neurology nurse practitioner, and a seizure diary<br>Comparator: treatment as usual | 54 (SD NR)<br>% Female NR<br>Race:<br>68.4% White<br>Marital status: NR | 50% employed<br>Epilepsy type: NR<br>Time since diagnosis: NR<br>Seizure frequency: NR | Seizure rate/frequency<br>Seizure severity<br>QOL: QOLIE-31*<br>Primary outcome: QOLIE-31<br>Timing: Pre-intervention and 12 months post-implementation | Objective: NA<br>Patient-reported: High |
| Haut, 2018[50]<br>USA<br>67<br>2 | Inclusion: Age ≥18, medication resistant (≥4 seizures during 56-day baseline period), stable AED regimen; awareness of triggers, premonitory features, and/or ability to self-predict seizures, focal epilepsy, able to maintain e-diary<br>Exclusion: suicide attempt within 2 years or suicidal ideation, status epilepticus w/in 6 months; stress reduction intervention | No acronym<br>Intervention was primarily stress management practice through PMR, with additional self-monitoring component based on seizure activity; patients received an in-person training session with a psychologist for PMR, and a follow-up training 6 weeks later<br>Comparator: Active focused-attention | 37.2 (SD 24)<br>62.5% female<br>Race: NR<br>Marital status: NR | Employment: NR<br>Focal: 64<br>Mean time since diagnosis: 26 years (SD 13.7)<br>Mean seizure frequency: 11.42/month (SD 15.83) | Anxiety symptoms<br>Depressive symptoms<br>Distress symptoms<br>Seizure frequency<br>Primary outcome: Seizure frequency<br>Timing: daily for 12 weeks | Objective: NA<br>Patient-reported: Low |

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| | w/in 3 months or failed prior stress reduction | | | | | |
| Helgeson,1990[51]<br>USA<br>100<br>2 | Inclusion: Epilepsy diagnosis and receiving AEDs<br>Exclusion: Mentally retarded, demented, or psychotic patients | Sepulveda Epilepsy Education program (SEE)<br>Psychoeducational treatment program providing education and psychosocial therapy through cognitive-behavioral methods to patients and their families; presented education on medical and compliance issues with epilepsy, and modeled skills for identifying and coping with psychological, social, family, and work-related problems of epilepsy<br>Comparator: waitlist | 37.3 (SD 11.85)<br>74% Female<br>Race: NR<br>Marital status: NR<br>Med adherence: NR | Employment: NR<br>Focal: 11<br>Generalized: 12<br>Mean time since diagnosis: 16.5 years (SD 10.95)<br>Mean seizure frequency: 2.3/month (SD 4.35) | Anxiety symptoms<br>Depressive symptoms<br>Seizure rate/frequency<br>Social functioning: Washington Psychosocial Seizure Inventory<br>Disease knowledge<br>Self-efficacy: Sherer self-efficacy scale<br>Primary outcome: NR<br>Timing: Baseline and 4 months | Objective: High<br>Patient-reported: High |
| Leenen, 2018[52]<br>Europe<br>103<br>2 | Inclusion: Adult patients with epilepsy using AED; understood Dutch; could participate in sessions/e-health devices<br>Exclusion: Unwilling or unable to participate in group sessions or felt to be unable to comprehend the topics discussed in sessions | ZMILE<br>Group sessions led by nurse practitioners aimed at improving knowledge, recognition, self-monitoring, and proactive coping<br>Comparator: treatment as usual | 41.7 (SD 14.7)<br>51% female<br>Race: NR<br>51% married | 34.3% employed<br>Epilepsy type: NR<br>Mean time since diagnosis: 20.1 years (SD 15.01)<br>Mean seizure frequency: 5.1/4 weeks (SD 11.15) | Anxiety symptoms<br>Depressive symptoms<br>Seizure rate/frequency<br>Seizure severity<br>QOL: QOLIE-31<br>Medication toxicity<br>Medication adherence: MARS<br>Self-efficacy: ESES | Objective: NA<br>Patient-reported: Low |

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| | | | | | Primary outcome: ESES<br>Timing: Baseline, 3 months, 6 months | |
| May, 2002[53]<br>Europe<br>383<br>2 | Inclusion: Patients with epilepsy age ≥16 who agreed to participate<br>Exclusion: Mental retardation, acute psychiatric illness; non-epileptic seizures only | MOSES (Modular Service Package Epilepsy)<br>Intervention involved discussion of factors: education about epilepsy; ways to emotionally cope with epilepsy, monitor symptoms and seizures, plan for or actively cope with pre-seizure symptoms/auras, and cooperating with clinicians and taking medications as prescribed<br>Comparator: waitlist | 38.0 (SD 13.59)<br>57% female<br>Race: NR<br>Marital status: NR | 41% employed<br>Focal: 152<br>Generalized: 43<br>Unknown seizure: 44<br>Median time since diagnosis: Arm 1: 13.5 years (IQR 4.7 to 26.2)<br>Arm 2: 18.2 years (IQR 8.5 to 29.6)<br>76% with at least 1 seizure in the past 6 months | Depressive symptoms<br>Seizure rate/frequency<br>Social functioning: Restrictions in daily living<br>QOL: SF36<br>Disease knowledge<br>Self-management: Coping with Epilepsy<br>Primary outcome: Restrictions in daily living, SF36, disease knowledge, Coping with Epilepsy<br>Timing: Baseline, 6 months post-course completion | Objective: NA<br>Patient-reported: High |
| McLaughlin, 2011[54]<br>Australia<br>37<br>2 | Inclusion: English-speaking adults, age ≥60 with confirmed diagnosis of epilepsy, who were able to attend weekly group sessions; must have | No acronym<br>A manualized, in-person, group CBT intervention delivered by a psychologist; self-management elements include psychoeducation, | 67.5 (SD 7.37)<br>51% female<br>Race: NR<br>Marital status: NR | Employment: NR<br>Focal: 20<br>Generalized: 17 | Depressive symptoms<br>Seizure rate/frequency<br>Social functioning: Washington | Objective: NA<br>Patient-reported: Unclear |

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| | MMSE ≥24, and able to provide information on physical and medical status | seizure diaries, CBT to reduce triggers, physical and emotional wellness (including medication management), seizure management<br>Comparator: active relaxation | | Mean time since diagnosis: 27.2 years (SD 27.22)<br>Seizure frequency: NR | Psychosocial Seizure Inventory<br>Primary Outcome: NR<br>Timing: 6 weeks, 3 months | |
| Puskarich, 1992[55]<br>USA<br>53<br>2 | Inclusion: Epilepsy diagnosis, 6 seizures during a run-in 8 week period with awareness of every seizure by self or witness, normal intellectual function, English-speaking | No acronym<br>Progressive muscle relaxation training; Subjects were encouraged to practice the relaxation techniques at home twice a day for 20 min<br>Comparator: quiet sitting | 39.4 (SD NR)<br>67% female<br>Race:<br>62% white<br>Marital status: NR | Employment: NR<br>Focal: 21<br>Generalized: 3<br>Mean time since diagnosis<br>22 years (SD NR)<br>Seizure frequency: NR | Seizure rate<br>Primary outcome: Seizure rate<br>Timing: 8 weeks | Objective: NA<br>Patient-reported: High |

| **Study<br>Country<br># Enrolled<br># Arms** | **Eligibility** | **Study Acronym<br>Intervention<br>Comparator** | **Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence** | **Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency** | **Outcomes Reported<br>Primary Outcome<br>Timing** | **Risk of Bias** |
|---|---|---|---|---|---|---|
| Ridsdale, 2018[57]<br>Europe<br>404<br>2 | Inclusion: Age ≥16 with epilepsy ≥1 year, diagnosed by specialist, on AED, ≥2 seizures in past year, understand English; able to attend 2-day course<br>Exclusion: Psychogenic seizures; substance misuse; serious psych illness; terminal illness | SMILE-UK (Self-management education for adults with poorly controlled epilepsy)<br>Intervention based on MOSES. 9 module group education; focused on patients with epilepsy, caregivers also invited<br>Comparator: treatment as usual | 41.7 (SD 14.1)<br>54.2% female<br>Race:<br>75.2% White<br>38.1% married | 41.8% employed<br>Epilepsy type: NR<br>Median time since diagnosis: 18 (IQR 8 to 32)<br>Median seizure frequency: 34/last 12 months (IQR 18 to 63) | Anxiety symptoms<br>Depressive symptoms<br>Seizure rate/frequency<br>QOL: QOLIE-31<br>Medication toxicity<br>Medication adherence: ESMS<br>Self-efficacy: Self-Mastery and Control scale<br>Primary outcome: QOLIE-31<br>Timing: Baseline, 6 months, 12 months | Objective: NA<br>Patient-reported: Low |
| Sajatovic, 2018[58]<br>USA<br>120<br>2 | Inclusion: Self-reported epilepsy, age ≥18, ≥1 negative health event (seizure, accident or traumatic injury, self-harm attempt, ED visit or hospitalization) in past 6 months<br>Exclusion: Immediate risk of self-harm; dementia; pregnancy; unable to read/understand English | SMART (Self-management for people with epilepsy)<br>Group-based, in-person, 60- to 90-minute session delivered collaboratively by a nurse educator-peer educator dyad. Then, 7 group format sessions delivered ~weekly via the internet on computer tablets using posters/graphics and emphasizing interactive discussion. Following the group sessions, 6 telephone maintenance sessions | 41.3 (SD 11.8)<br>68.1% female<br>Race:<br>30.1% White<br>31.7% married | 25.8% employed<br>Focal: 4<br>Generalized: 85<br>Mean time since diagnosis: 20.6 (SD 15.2)<br>Seizure frequency: 2.2/30 days (SD 4.9) | Depressive symptoms<br>Seizure rate/frequency<br>Seizure severity<br>QOL: QOLIE-10<br>Negative health events<br>Self-efficacy: ESES<br>Self-management: ESMS<br>ED visit for epilepsy<br>Hospitalization f(any cause) | Objective: Unclear<br>Patient-reported: Unclear |

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| | | (approximately every 2 weeks) with the peer educator and the nurse educator alternating calls.<br>Comparator: Waitlist control group, allowed to continue treatment as usual with providers, and received intervention after 6-month follow-up with treatment group. | | | Primary outcome: change in total negative health events<br>Timing: 24 weeks | |
| Tan, 1986[56]<br>Canada<br>30<br>3 | Inclusion: Adult epilepsy patients with significant psychosocial problems and inadequate seizure control (as judged by neurologist)<br>Exclusion: Mentally retarded; psychotic | No acronym<br>CBT based intervention that included education via explicit readings; symptom monitoring for seizures, problem solving of anticipated seizure-related issues in life; stress management; increasing other healthy activities<br>Comparators: CBT vs supportive counseling vs waitlist | 33.4 (SD 11.1)<br>63% female<br>Race: NR<br>Marital status: NR | Employment: NR<br>Focal: 22<br>Generalized: 5<br>Mean time since diagnosis: 15.5 (SD 8.9)<br>Seizure frequency: NR | Depressive symptoms<br>Seizure rate/frequency<br>Social functioning: Washington Psychosocial Seizure Inventory<br>Medication adherence: “Compliance with Taking Anticonvulsant Meds” Likert scale 1-5<br>Primary outcome: NR<br>Timing: pre-intervention, post- | Objective: NA<br>Patient-reported: High |

| Study<br>Country<br># Enrolled<br># Arms | Eligibility | Study Acronym<br>Intervention<br>Comparator | Mean Age<br>% Female<br>% Race<br>Marital Status<br>Medication Adherence | Occupational Status<br>Epilepsy Type<br>Time Since Diagnosis<br>Seizure Frequency | Outcomes Reported<br>Primary Outcome<br>Timing | Risk of Bias |
|---|---|---|---|---|---|---|
| | | | | | intervention, 4 months | |

Abbreviations: AED=antiepileptic drug; CBT=cognitive behavioral therapy; ED=emergency department; ESES= Epilepsy Self-Efficacy Scale; ESMS=Epilepsy Self-Management Scale; IQR=interquartile range; MMSE=Mini-Mental State Examination; MOCA=Montreal Cognitive Assessment; MOSES=Modular Service Package Epilepsy; NA=not applicable; NR=not reported; SD=standard deviation

# APPENDIX E. EXCLUDED STUDIES

| Study | Not full publication | Not eligible country | Not population of interest | Not eligible setting | Not eligible intervention | Not eligible design | Not eligible outcome |
|---|---|---|---|---|---|---|---|
| Aliasgharpour, 2013[1] | | X | | | | | |
| Caller, 2016[2] | X | | | | | | |
| Cervenka, 2012[3] | | | | | X | | |
| Chappell, 1999[4] | | | | | X | | |
| Clark, 2001[5] | | | X | | | | |
| Cole, 2015[6] | | | | | X | | |
| Collard, 2017[7] | | | | | | X | |
| Crooks, 2017[8] | | | X | | | | |
| Davis, 2004[9] | | | | X | | | |
| De Barros, 2018[10] | | | X | | | | |
| DiIorio, 2011[11] | X | | | | | | |
| DiIorio, 2009[12] | | | | | | X | |
| DiIorio, 2009[13] | | | | | | X | |
| DiIorio, 1992[14] | | | | | X | | |
| Elsas, 2011[15] | | | | | | X | |
| Endermann, 2015[16] | | | X | | | | |
| Engelberts, 2002[17] | | | | | X | | |
| Groenewegen, 2014[18] | | | | X | | | |
| Helde, 2003[19] | | | | | X | | |
| Helde, 2005[20] | | | | | X | | |
| Helmstaedter, 2008[21] | | | | | X | | |
| Hixson, 2015[22] | | | | | | X | |
| Hixson, 2015[23] | | | | X | | | |
| Kobau, 2003[24] | | | | X | | | |
| Kotchoubey, 2001[25] | | | | | | X | |
| Krakow, 1999[26] | | | | X | | | |
| Kralj-Hans, 2014[27] | | | | | X | | |
| Kumar, 2018[28] | | | | | X | | |

| Study | Not full publication | Not eligible country | Not population of interest | Not eligible setting | Not eligible intervention | Not eligible design | Not eligible outcome |
|---|---|---|---|---|---|---|---|
| Lai, 2018[29] | | X | | | | | |
| Leenen, 2014[30] | | | | X | | | |
| Losada-Camacho, 2014[31] | | X | | | | | |
| Lua, 2013[32] | | X | | | | | |
| Lundgren, 2008[33] | | X | | | | | |
| Lundgren, 2006[34] | | X | | | | | |
| Martinovic, 2001[35] | | X | | | | | |
| McAuley, 2001[36] | | | | | X | | |
| Mejdahl, 2017[37] | | | | | X | | |
| Minshall, 2008[38] | | | X | | | | |
| Mody, 2016[39] | | | | | X | | |
| Myers, 2017[40] | | | | X | | | |
| Newman, 2016[41] | | | | | | X | |
| Noble, 2014[42] | | | | | | X | |
| Ogata, 2000[43] | | | | | X | | |
| Pakpour, 2015[44] | | X | | | | | |
| Peterson, 1984[45] | | | | | X | | |
| Peterson, 1982[46] | | | | | X | | |
| Pfeifer, 2005[47] | | | | | X | | |
| Pramuka, 2007[48] | | | | | | X | |
| Privitera, 2014[49] | | | | | X | | |
| Radford, 2011[50] | | | | | X | | |
| Rajesh, 2006[51] | | X | | | | | |
| Ridsdale, 2013[52] | | | | | | X | |
| Ridsdale, 2002[53] | | | X | | | | |
| Ridsdale, 2000[54] | | | | | X | | |
| Ridsdale, 1999[55] | | | | | X | | |
| Ridsdale, 1996[56] | | | | X | | | |
| Rockstroh, 1993[57] | | | | | X | | |
| Roth, 1994[58] | | | | | X | | |

| Study | Not full publication | Not eligible country | Not population of interest | Not eligible setting | Not eligible intervention | Not eligible design | Not eligible outcome |
|---|---|---|---|---|---|---|---|
| Sahoo, 2016[59] | | | | | X | | |
| Sajatovic, 2017[60] | | | | | | X | |
| Saramma, 2014[61] | | X | | | | | |
| Sathyaprabha, 2008[62] | | X | | | | | |
| Sawangchareon, 2013[63] | | X | | | | | |
| Schougaard, 2017[64] | | | | | | X | |
| Schroder, 2014[65] | | | | | X | | |
| Schröder, 2014[66] | | | | | X | | |
| Shaw, 2010[67] | X | | | | | | |
| Shaw, 2007[68] | | | | | | X | |
| Shegog, 2017[69] | | | | | | X | |
| Smith, 2017[70] | | | | | | X | |
| Smithson, 2013[71] | | | | | X | | |
| Spector, 1999[72] | | | | | | X | |
| Staniszewska, 2017[73] | | | | | X | | |
| Strehl, 2014[74] | | | | | | X | |
| Sung, 2017[75] | | | X | | | | |
| Tang, 2015[76] | | X | | | | | |
| Tatum, 2008[77] | | | | | X | | |
| Thompson, 2010[78] | | | X | | | | |
| Trostle, 1983[79] | | | | | X | | |
| CDC Epilepsy Program[80] | | | | | X | | |
| Walker, 2010[81] | | | X | | | | |
| Walker, 2009[82] | | | | | | X | |
| Wood, 2017[83] | | | | | | X | |
| Yardi, 2001[84] | | | | | | X | |

## REFERENCES TO APPENDIX E

1. Aliasgharpour M, Dehgahn Nayeri N, Yadegary MA, et al. Effects of an educational program on self-management in patients with epilepsy. *Seizure*. 2013;22(1):48-52.
2. Caller T, Ferguson R, Roth R, et al. Self-management (HOBSCOTCH) improves cognition and quality of life in epilepsy: a randomized controlled trial. *Neurology*. Vol. 86; 2016.
3. Cervenka MC, Terao NN, Bosarge JL, et al. E-mail management of the modified Atkins Diet for adults with epilepsy is feasible and effective. *Epilepsia*. 2012;53(4):728-32.
4. Chappell B, Smithson H. Meeting the educational needs of general practitioners for epilepsy. *Seizure*. 1999;8(3):157-62.
5. Clark AJ, Espie CA, Paul A. Adults with learning disabilities and epilepsy: knowledge about epilepsy before and after an educational package. *Seizure*. 2001;10(7):492-9.
6. Cole KA, Gaspar PM. Implementation of an epilepsy self-management protocol. *J Neurosci Nurs*. 2015;47(1):3-9.
7. Collard SS, Ellis-Hill C. How do you exercise with epilepsy? Insights into the barriers and adaptations to successfully exercise with epilepsy. *Epilepsy Behav*. 2017;70(Pt A):66-71.
8. Crooks RE, Bell M, Patten SB, et al. Mind the gap: Exploring information gaps for the development of an online resource hub for epilepsy and depression. *Epilepsy Behav*. 2017;70(Pt A):18-23.
9. Davis J, Roberts R, Davidson DL, et al. Implementation strategies for a Scottish national epilepsy guideline in primary care: results of the Tayside Implementation of Guidelines in Epilepsy Randomized (TIGER) trial. *Epilepsia*. 2004;45(1):28-34.
10. de Barros ACS, Furlan AER, Marques LHN, et al. Effects of a psychotherapeutic group intervention in patients with refractory mesial temporal lobe epilepsy and comorbid psychogenic nonepileptic seizures: A nonrandomized controlled study. *Seizure*. 2018;58:22-28.
11. DiIorio C, Bamps Y, Walker E. Results of a randomized controlled trial evaluating webease, an online self-management program. *Epilepsy currents*. Vol. 11; 2011.
12. DiIorio C, Reisinger EL, Yeager KA, et al. A telephone-based self-management program for people with epilepsy. *Epilepsy Behav*. 2009;14(1):232-6.
13. DiIorio C, Escoffery C, McCarty F, et al. Evaluation of WebEase: an epilepsy self-management Web site. *Health Educ Res*. 2009;24(2):185-97.
14. DiIorio C, Faherty B, Manteuffel B. Self-efficacy and social support in self-management of epilepsy. *West J Nurs Res*. 1992;14(3):292-303; discussion 303-7.
15. Elsas SM, Gregory WL, White G, et al. Aura interruption: the Andrews/Reiter behavioral intervention may reduce seizures and improve quality of life - a pilot trial. *Epilepsy Behav*. 2011;22(4):765-72.
16. Endermann M. Rehabilitation for young adults with epilepsy and mild intellectual disabilities: results of a prospective study with repeated measurements. *Seizure*. 2015;26:72-80.
17. Engelberts NH, Klein M, Ader HJ, et al. The effectiveness of cognitive rehabilitation for attention deficits in focal seizures: a randomized controlled study. *Epilepsia*. 2002;43(6):587-95.

18. Groenewegen A, Tofighy A, Ryvlin P, et al. Measures for improving treatment outcomes for patients with epilepsy--results from a large multinational patient-physician survey. *Epilepsy Behav*. 2014;34:58-67.
19. Helde G, Brodtkorb E, Brathen G, et al. An easily performed group education programme for patients with uncontrolled epilepsy--a pilot study. *Seizure*. 2003;12(7):497-501.
20. Helde G, Bovim G, Brathen G, et al. A structured, nurse-led intervention program improves quality of life in patients with epilepsy: a randomized, controlled trial. *Epilepsy Behav*. 2005;7(3):451-7.
21. Helmstaedter C, Loer B, Wohlfahrt R, et al. The effects of cognitive rehabilitation on memory outcome after temporal lobe epilepsy surgery. *Epilepsy Behav*. 2008;12(3):402-9.
22. Hixson JD, Barnes D, Parko K, et al. Patients optimizing epilepsy management via an online community: the POEM Study. *Neurology*. 2015;85(2):129-36.
23. Hixson JD, Van Bebber SL, Bertko KM. Interest in a digital health tool in veterans with epilepsy: results of a phone survey. *Mil Med*. 2015;180(4):387-90.
24. Kobau R, DiIorio C. Epilepsy self-management: a comparison of self-efficacy and outcome expectancy for medication adherence and lifestyle behaviors among people with epilepsy. *Epilepsy Behav*. 2003;4(3):217-25.
25. Kotchoubey B, Strehl U, Uhlmann C, et al. Modification of slow cortical potentials in patients with refractory epilepsy: a controlled outcome study. *Epilepsia*. 2001;42(3):406-16.
26. Krakow K, Buhler K, Haltenhof H. Coping with refractory epilepsy. *Seizure*. 1999;8(2):111-5.
27. Kralj-Hans I, Goldstein LH, Noble AJ, et al. Self-Management education for adults with poorly controlled epILEpsy (SMILE (UK)): a randomised controlled trial protocol. *BMC Neurol*. 2014;14:69.
28. Kumar N, Colon-Zimmermann K, Fuentes-Casiano E, et al. Clinical correlates of negative health events in a research sample with epilepsy. *Epilepsy Behav*. 2018;79:225-229.
29. Lai ST, Lim KS, Tang V, et al. Positive psychological interventions for people with epilepsy: An assessment on factors related to intervention participation. *Epilepsy Behav*. 2018;80:90-97.
30. Leenen LA, Wijnen BF, de Kinderen RJ, et al. (Cost)-effectiveness of a multi-component intervention for adults with epilepsy: study protocol of a Dutch randomized controlled trial (ZMILE study). *BMC Neurol*. 2014;14:255.
31. Losada-Camacho M, Guerrero-Pabon MF, Garcia-Delgado P, et al. Impact of a pharmaceutical care programme on health-related quality of life among women with epilepsy: a randomised controlled trial (IPHIWWE study). *Health Qual Life Outcomes*. 2014;12:162.
32. Lua PL, Neni WS. A randomised controlled trial of an SMS-based mobile epilepsy education system. *J Telemed Telecare*. 2013;19(1):23-8.
33. Lundgren T, Dahl J, Yardi N, et al. Acceptance and Commitment Therapy and yoga for drug-refractory epilepsy: a randomized controlled trial. *Epilepsy Behav*. 2008;13(1):102-8.
34. Lundgren T, Dahl J, Melin L, et al. Evaluation of acceptance and commitment therapy for drug refractory epilepsy: a randomized controlled trial in South Africa--a pilot study. *Epilepsia*. 2006;47(12):2173-9.

35. Martinovic Z. Adjunctive behavioural treatment in adolescents and young adults with juvenile myoclonic epilepsy. *Seizure*. 2001;10(1):42-7.
36. McAuley JW, Long L, Heise J, et al. A Prospective Evaluation of the Effects of a 12-Week Outpatient Exercise Program on Clinical and Behavioral Outcomes in Patients with Epilepsy. *Epilepsy Behav*. 2001;2(6):592-600.
37. Mejdahl CT, Schougaard LMV, Hjollund NH, et al. PRO-based follow-up as a means of self-management support - an interpretive description of the patient perspective. *J Patient Rep Outcomes*. 2017;2:38.
38. Minshall I, Smith D. The impact of a citywide audit with educational intervention on the care of patients with epilepsy. *Seizure*. 2008;17(3):261-8.
39. Mody SK, Haunschild C, Farala JP, et al. An educational intervention on drug interactions and contraceptive options for epilepsy patients: a pilot randomized controlled trial. *Contraception*. 2016;93(1):77-80.
40. Myers L, Lancman M, Laban-Grant O, et al. Socialization characteristics in persons with epilepsy. *Epilepsy Behav*. 2017;72:99-107.
41. Newman C, Shankar R, Hanna J, et al. Developing an Evidence-Based Epilepsy Risk Assessment eHealth Solution: From Concept to Market. *JMIR Res Protoc*. 2016;5(2):e82.
42. Noble AJ, McCrone P, Seed PT, et al. Clinical- and cost-effectiveness of a nurse led self-management intervention to reduce emergency visits by people with epilepsy. *PLoS One*. 2014;9(6):e90789.
43. Ogata A, Amano K. A psychosocial approach to epileptic patients. *Epilepsia*. 2000;41 Suppl 9:36-8.
44. Pakpour AH, Gholami M, Esmaeili R, et al. A randomized controlled multimodal behavioral intervention trial for improving antiepileptic drug adherence. *Epilepsy Behav*. 2015;52(Pt A):133-42.
45. Peterson GM, McLean S, Millingen KS. A randomised trial of strategies to improve patient compliance with anticonvulsant therapy. *Epilepsia*. 1984;25(4):412-7.
46. Peterson GM, McLean S, Millingen KS. Determinants of patient compliance with anticonvulsant therapy. *Epilepsia*. 1982;23(6):607-13.
47. Pfeifer HH, Thiele EA. Low-glycemic-index treatment: a liberalized ketogenic diet for treatment of intractable epilepsy. *Neurology*. 2005;65(11):1810-2.
48. Pramuka M, Hendrickson R, Zinski A, et al. A psychosocial self-management program for epilepsy: a randomized pilot study in adults. *Epilepsy Behav*. 2007;11(4):533-45.
49. Privitera M, Walters M, Lee I, et al. Characteristics of people with self-reported stress-precipitated seizures. *Epilepsy Behav*. 2014;41:74-7.
50. Radford K, Lah S, Thayer Z, et al. Effective group-based memory training for patients with epilepsy. *Epilepsy Behav*. 2011;22(2):272-8.
51. Rajesh B, Jayachandran D, Mohandas G, et al. A pilot study of a yoga meditation protocol for patients with medically refractory epilepsy. *J Altern Complement Med*. 2006;12(4):367-71.
52. Ridsdale L, McCrone P, Morgan M, et al. Health Services and Delivery Research. Can an epilepsy nurse specialist-led self-management intervention reduce attendance at emergency departments and promote well-being for people with severe epilepsy? A non-randomised trial with a nested qualitative phase. Southampton (UK): NIHR Journals Library.
53. Ridsdale L, Kwan I, Morgan M. How can a nurse intervention help people with newly diagnosed epilepsy? A qualitative study (of patients' views). *Seizure*. 2002;11(1):1-5.

54. Ridsdale L, Kwan I, Cryer C. Newly diagnosed epilepsy: can nurse specialists help? A randomized controlled trial. Epilepsy Care Evaluation Group. *Epilepsia*. 2000;41(8):1014-9.
55. Ridsdale L, Kwan I, Cryer C. The effect of a special nurse on patients' knowledge of epilepsy and their emotional state. Epilepsy Evaluation Care Group. *Br J Gen Pract*. 1999;49(441):285-9.
56. Ridsdale L, Robins D, Fitzgerald A, et al. Epilepsy monitoring and advice recorded: general practitioners' views, current practice and patients' preferences. *Br J Gen Pract*. 1996;46(402):11-4.
57. Rockstroh B, Elbert T, Birbaumer N, et al. Cortical self-regulation in patients with epilepsies. *Epilepsy Res*. 1993;14(1):63-72.
58. Roth DL, Goode KT, Williams VL, et al. Physical exercise, stressful life experience, and depression in adults with epilepsy. *Epilepsia*. 1994;35(6):1248-55.
59. Sahoo SS, Ramesh P, Welter E, et al. Insight: An ontology-based integrated database and analysis platform for epilepsy self-management research. *Int J Med Inform*. 2016;94:21-30.
60. Sajatovic M, Jobst BC, Shegog R, et al. The Managing Epilepsy Well Network:: Advancing Epilepsy Self-Management. *Am J Prev Med*. 2017;52(3s3):S241-s245.
61. Saramma PP, Sarma PS, Thomas SV. Effect of a self-instructional module on the child rearing knowledge and practice of women with epilepsy. *Seizure*. 2014;23(6):424-8.
62. Sathyaprabha TN, Satishchandra P, Pradhan C, et al. Modulation of cardiac autonomic balance with adjuvant yoga therapy in patients with refractory epilepsy. *Epilepsy Behav*. 2008;12(2):245-52.
63. Sawangchareon K, Pranboon S, Tiamkao S, et al. Moving the self-esteem of people with epilepsy by supportive group: a clinical trial. *J Caring Sci*. 2013;2(4):329-35.
64. Schougaard LM, Mejdahl CT, Petersen KH, et al. Effect of patient-initiated versus fixed-interval telePRO-based outpatient follow-up: study protocol for a pragmatic randomised controlled study. *BMC Health Serv Res*. 2017;17(1):83.
65. Schroder J, Bruckner K, Fischer A, et al. Efficacy of a psychological online intervention for depression in people with epilepsy: a randomized controlled trial. *Epilepsia*. 2014;55(12):2069-76.
66. Schröder J, Brückner K, Fischer A, et al. Efficacy of a psychological online intervention for depression in people with epilepsy: a randomized controlled trial. *Epilepsia*. Vol. 55; 2014:2069-2076.
67. Shaw EJ, Stokes T, Camosso-Stefinovic J, et al. WITHDRAWN: Self-management education for adults with epilepsy. *Cochrane Database Syst Rev*. 2010(10):Cd004723.
68. Shaw EJ, Stokes T, Camosso-Stefinovic J, et al. Self-management education for adults with epilepsy. *Cochrane Database Syst Rev*. 2007(2):Cd004723.
69. Shegog R, Begley CE. Clinic-Based Mobile Health Decision Support to Enhance Adult Epilepsy Self-Management: An Intervention Mapping Approach. *Front Public Health*. 2017;5:256.
70. Smith A, McKinlay A, Wojewodka G, et al. A systematic review and narrative synthesis of group self-management interventions for adults with epilepsy. *BMC Neurol*. 2017;17(1):114.
71. Smithson WH, Hukins D, Buelow JM, et al. Adherence to medicines and self-management of epilepsy: a community-based study. *Epilepsy Behav*. 2013;26(1):109-13.

72. Spector S, Tranah A, Cull C, et al. Reduction in seizure frequency following a short-term group intervention for adults with epilepsy. *Seizure*. 1999;8(5):297-303.
73. Staniszewska A, Smolenska E, Religioni U. Health Behaviors Related to the Use of Drugs among Patients with Epilepsy. *Am J Health Behav*. 2017;41(4):511-517.
74. Strehl U, Birkle SM, Worz S, et al. Sustained reduction of seizures in patients with intractable epilepsy after self-regulation training of slow cortical potentials - 10 years after. *Front Hum Neurosci*. 2014;8:604.
75. Sung C, Lin CC, Connor A, et al. Disclose or not? Effect of impression management tactics on hireability of persons with epilepsy. *Epilepsia*. 2017;58(1):128-136.
76. Tang V, Poon WS, Kwan P. Mindfulness-based therapy for drug-resistant epilepsy: An assessor-blinded randomized trial. *Neurology*. 2015;85(13):1100-7.
77. Tatum WOt, Al-Saadi S, Orth TL. Outpatient case management in low-income epilepsy patients. *Epilepsy Res*. 2008;82(2-3):156-61.
78. Thompson NJ, Walker ER, Obolensky N, et al. Distance delivery of mindfulness-based cognitive therapy for depression: project UPLIFT. *Epilepsy Behav*. 2010;19(3):247-54.
79. Trostle JA, Hauser WA, Susser IS. The logic of noncompliance: management of epilepsy from the patient's point of view. *Cult Med Psychiatry*. 1983;7(1):35-56.
80. U.S. Centers For Disease Control and Prevention Epilepsy Program. Internet use and looking up information online in adults with epilepsy varies by epilepsy status--2013 National Health Interview Survey. *Epilepsy Behav*. 2016;54:47-9.
81. Walker ER, Obolensky N, Dini S, et al. Formative and process evaluations of a cognitive-behavioral therapy and mindfulness intervention for people with epilepsy and depression. *Epilepsy Behav*. 2010;19(3):239-46.
82. Walker ER, Wexler B, DiIorio C, et al. Content and characteristics of goals created during a self-management intervention for people with epilepsy. *J Neurosci Nurs*. 2009;41(6):312-21.
83. Wood K, Lawrence M, Jani B, et al. Mindfulness-based interventions in epilepsy: a systematic review. *BMC Neurol*. 2017;17(1):52.
84. Yardi N. Yoga for control of epilepsy. *Seizure*. 2001;10(1):7-12.

# APPENDIX F. GLOSSARY

For full study citations in this appendix, please refer to the report's main reference list.

<table>
<tr><th>Term</th><th>Definition</th></tr>
<tr><td><b>Certainty of evidence (COE)</b></td><td>We assessed COE using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach[37] for 4 domains:
<table>
<tr><th><i>Domain</i></th><th><i>Rating</i></th><th><i>How Assessed</i></th></tr>
<tr><td>Risk of bias</td><td>Low<br>Unclear<br>High</td><td>Assessed primarily through study design and aggregate study quality</td></tr>
<tr><td>Consistency</td><td>Consistent<br>Inconsistent<br>Unknown/NA</td><td>Assessed primarily through whether effect sizes are generally on the same side of "no effect," the overall range of effect sizes, and statistical measures of heterogeneity</td></tr>
<tr><td>Directness</td><td>Direct<br>Indirect</td><td>Assessed by whether the evidence involves direct comparisons or indirect comparisons through use of surrogate outcomes or use of separate bodies of evidence</td></tr>
<tr><td>Precision</td><td>Precise<br>Imprecise</td><td>Based primarily on the size of the confidence intervals of effect estimates, the optimal information size and considerations of whether the confidence interval crossed the clinical decision threshold for using a therapy</td></tr>
</table>
Summary COE ratings for a body of evidence:
<ul>
<li>High—High confidence that the true effect lies close to that of the estimate of the effect.</li>
<li>Moderate—Moderate confidence 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.</li>
<li>Low—Limited confidence in the effect estimate. The true effect may be substantially different from the estimate of the effect.</li>
<li>Very low—Very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.</li>
<li>Insufficient—Impossible or imprudent to rate. In these situations, a rating of insufficient is assigned.</li>
</ul></td></tr>
<tr><td><b>Cognitive behavioral therapy (CBT)</b></td><td>Psychological treatment that addresses unhelpful ways of thinking and unhelpful behavior.</td></tr>
<tr><td><b>Hierarchical stress inoculation</b></td><td>Technique used to systematically desensitize individuals to anxiety-producing situations through conceptualizing and coping with increasing stress.</td></tr>
<tr><td><b>Objective outcomes (<i>ie</i>, non–patient-reported outcomes)</b></td><td>Measures that are not subject to a large degree of individual interpretation and are likely to be reliably measured across patients in a study, by different health care providers, and over time.</td></tr>
<tr><td><b>Patient-reported outcomes</b></td><td>Outcomes that are directly reported by the patient without interpretation of the patient's response by a clinician or anyone else and pertains to the patient's</td></tr>
</table>

| Term | Definition |
|---|---|
| | health, quality of life, or functional status associated with health care or treatment. |
| **Problem solving therapy (PST)** | Psychological treatment that teaches management of negative effects of stressful life events. Goals of PST include identifying types of stressors that trigger emotion and better understanding and management of negative emotions. |
| **Progressive muscle relaxation (PMR)** | A relaxation technique that involves tensing and relaxing muscle groups to reduce body tension. |
| **Risk of bias (ROB)** | An assessment of study quality. We used the following guidance in this report.<br>(1) For KQ 1 and KQ 2, we used the Cochrane EPOC ROB tool, which is applicable to randomized and nonrandomized studies[28]:<br>· Randomization and allocation concealment<br>· Comparability of groups at baseline<br>· Blinded outcomes assessment<br>· Completeness of follow-up and differential loss to follow-up<br>· Whether incomplete data were addressed appropriately<br>· Protection against contamination<br>· Selective outcomes reporting<br>Summary ROB ratings for a study:<br>· Low ROB—Bias, if present, is unlikely to alter the results seriously<br>· Unclear ROB—Bias that raises some doubts about the results<br>· High ROB—Bias that may alter the results seriously<br>(2) We used the Critical Appraisal Skills Programme (CASP) criteria to evaluate the ROB for qualitative study designs[30]:<br>· Clear statement of aims<br>· Appropriate qualitative methodology<br>· Appropriate research design<br>· Appropriate recruitment<br>· Appropriate data collection<br>· Consideration of ethical issues<br>· Sufficiently rigorous data analysis<br>· Clear statement of findings<br>· Valuable of the research<br>(3) We used the Mixed Methods Appraisal Tool (MMAT) 5 items specific to descriptive studies to evaluate the ROB for quantitative descriptive designs[31]:<br>· Relevant sampling strategy<br>· Representative sample<br>· Appropriate measures<br>· Risk of non-response bias<br>· Appropriate statistical analysis<br>We also used the MMAT 5 items for mixed methods to evaluate the ROB for mixed-methods studies[31]:<br>· Adequate rationale for using a mixed-methods design<br>· Effective integration of the different components<br>· Adequate interpretation of the integration of qualitative and quantitative comments |

| Term | Definition |
|---|---|
| | · Adequately addressed inconsistencies between quantitative and qualitative results<br>· Adherence of the different components to the quality criteria of each method<br>No summary ROB was possible for the CASP or MMAT. |
| **Standardized mean difference (SMD)** | The difference in outcomes between the intervention and comparator, divided by the pooled standard deviation. |