Evidence Synthesis Program

Self-management of Epilepsy:
A Systematic Review

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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.

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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.

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Deputy National Director of Neurology

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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
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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.

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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?

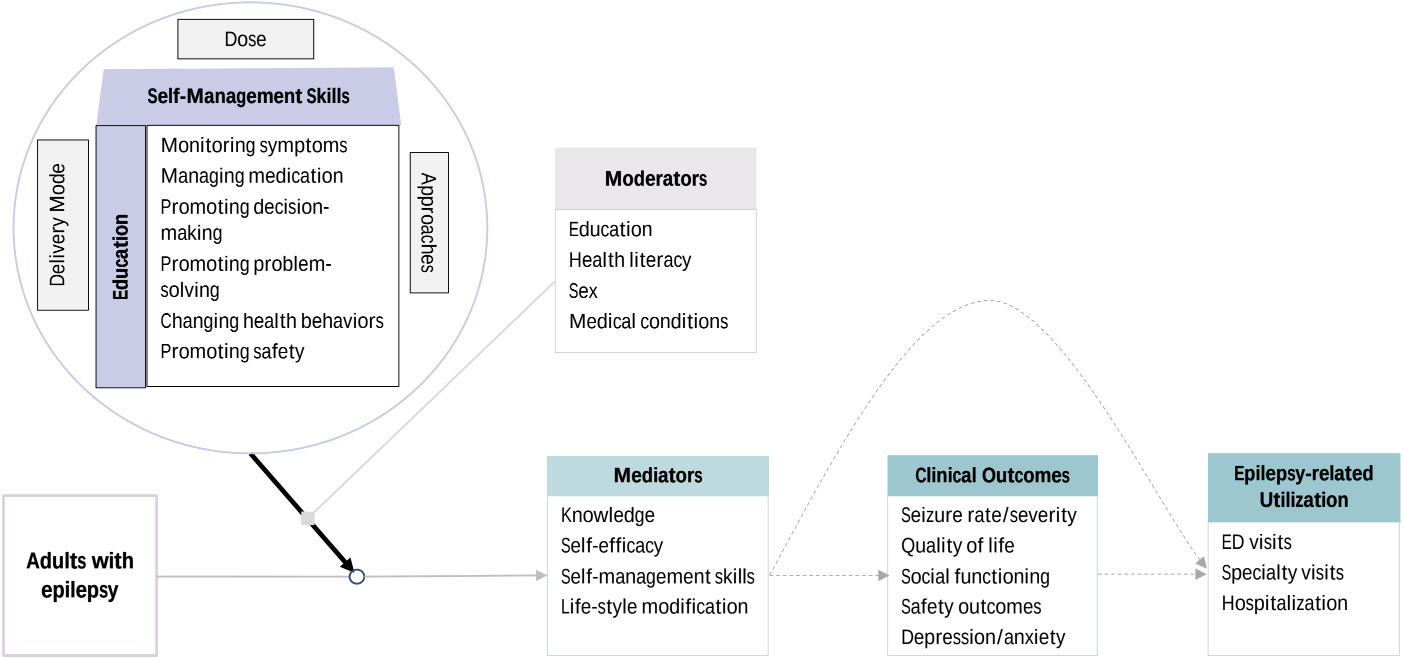
Conceptual Framework

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 · Family members and/or caregivers of those with epilepsy · KQ 3 only: Stakeholders involved in implementation (*eg*, neurologists, health coaches, nurses, administrators)	· Children · Populations with <70% adults · Severe learning disabilities · Non-epileptic seizures (*ie*, psychogenic seizures) · 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: · Stimulation of independent sign/symptom monitoring · Medication management · Enhancing problem-solving and decision-making skills for epilepsy treatment management, safety promotion (*eg*, driving) · 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 ● Cognitive behavioral therapy focused on comorbid mental illness in patients with epilepsy (*eg*, depression in patients with epilepsy) ● Education-only interventions ● General care delivery interventions (*eg*, introducing specialist nurse practitioner or implementation of clinical practice guidelines)

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

Study Characteristic	Include	Exclude
	KQ 3: ● Above KQ study designs ● Qualitative and survey designs if specifically addressing facilitators and barriers to adoption of epilepsy self-management interventions	● Systematic reviews/meta-analyses KQ 3: · 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

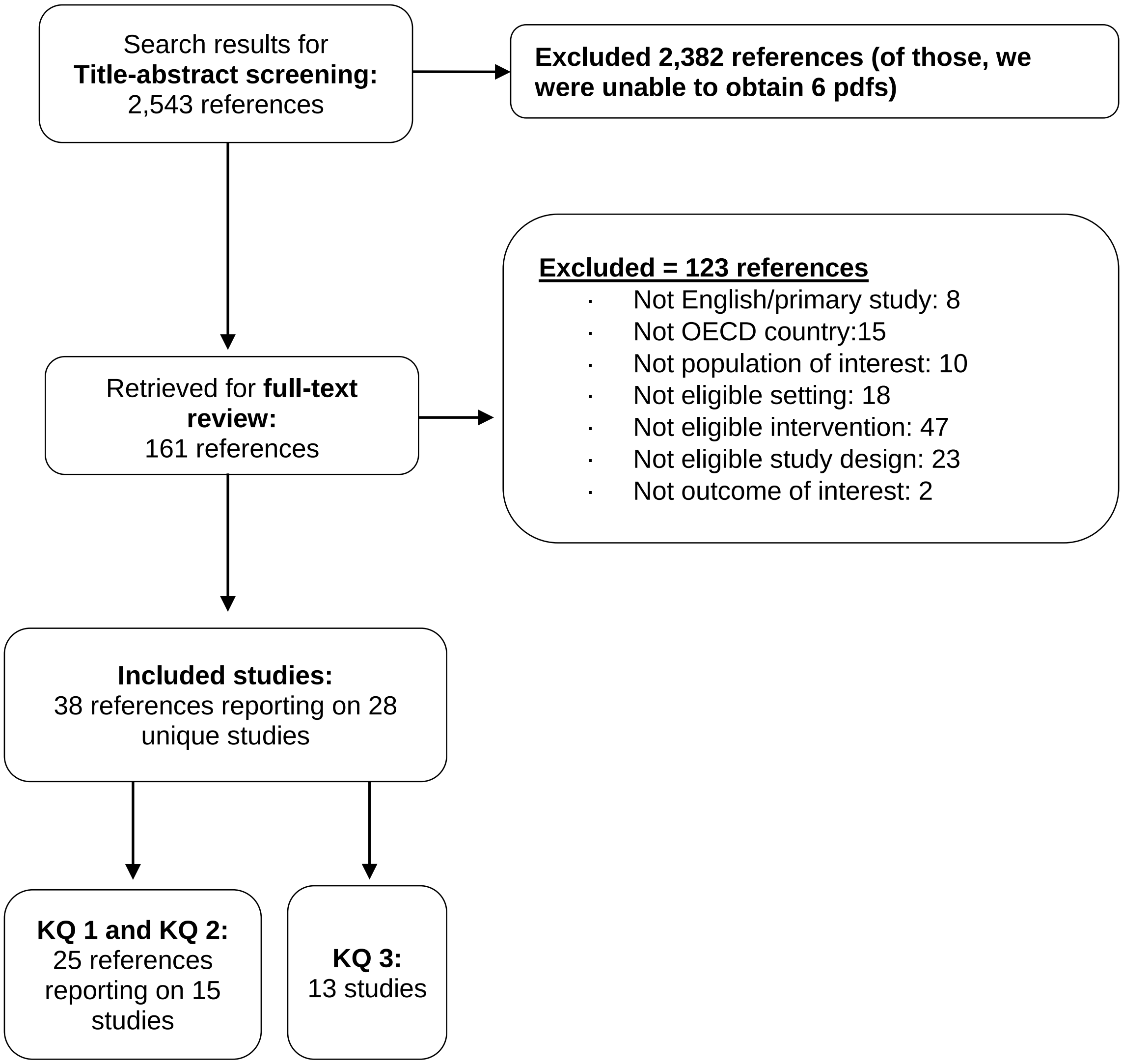
The results are organized to first report the yield of the literature search and the pattern of reported outcomes. Results are then reported for each KQ. For KQ 2, intervention effects are reported by category (*eg*, educational and psychosocial self-management interventions) and within the categories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

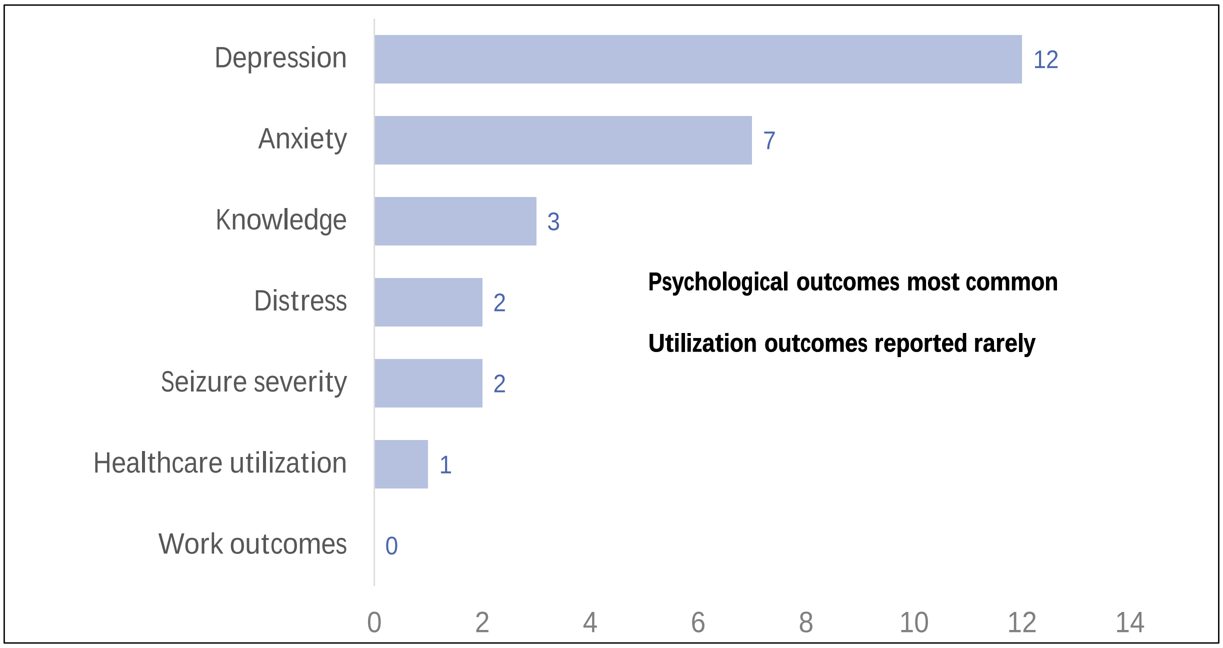


PATTERNS OF OUTCOME REPORTING

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)



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] WebEase Randomized	Y	Y	Y	Y	N	Y	5
Fraser, 2015[48] PACES Randomized	Y	N	Y	Y	N	Y	4
Helgeson,1990[51] SEE Randomized	Y	N	Y	Y	N	N	3
May, 2002[53] MOSES Randomized	Y	Y	Y	Y	N	N	4
Ridsdale, 2018[57]	Y	Y	N	Y	Y	Y	5

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

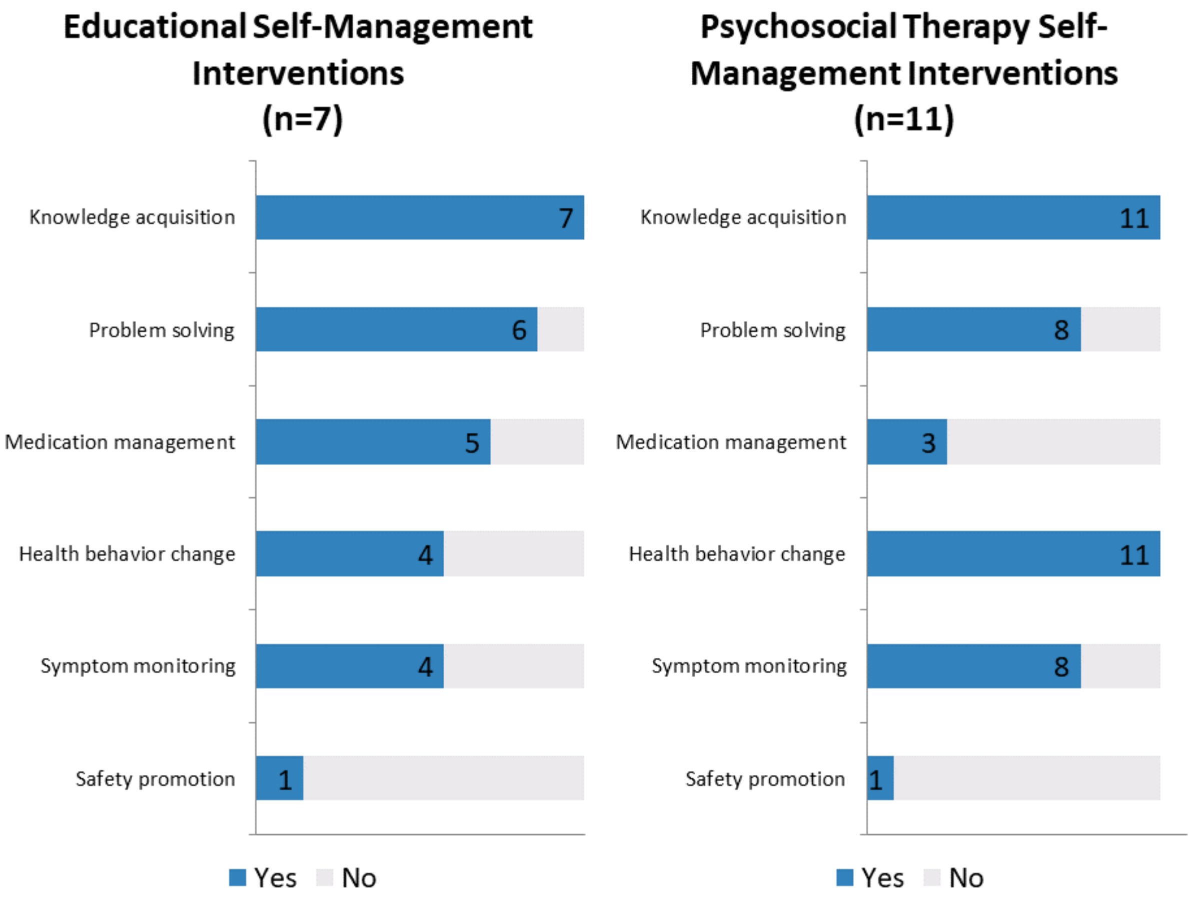
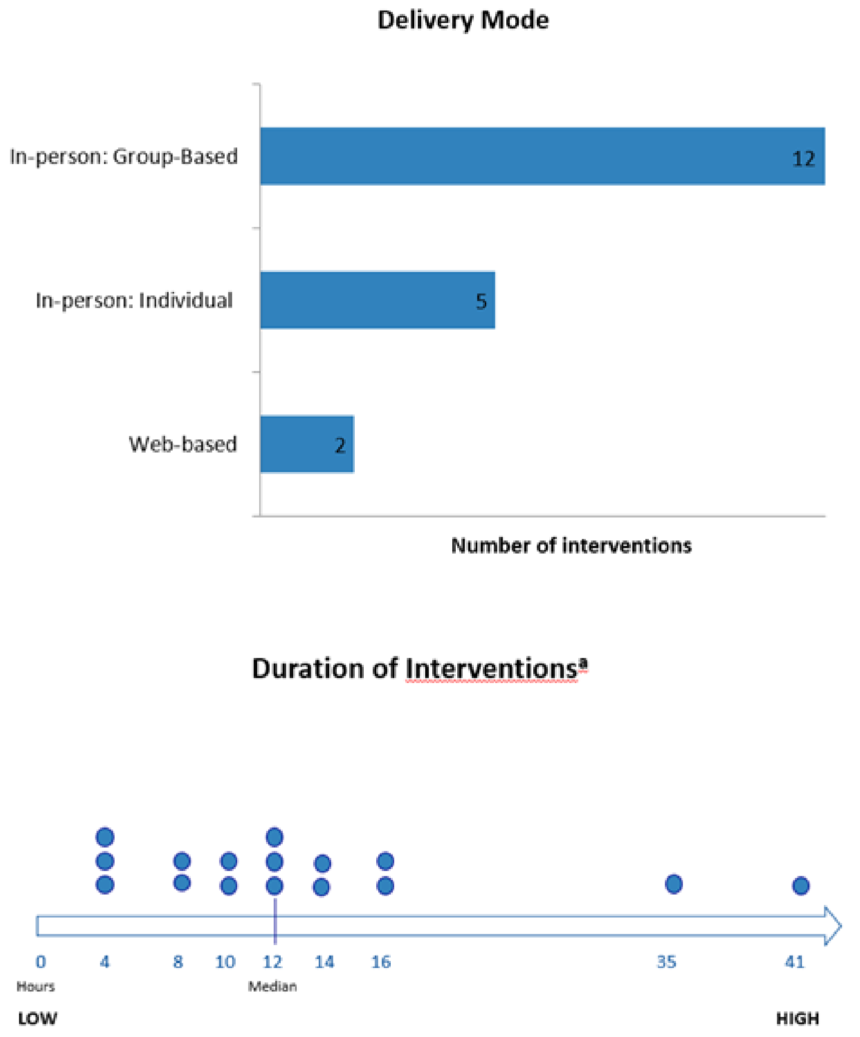


Figure 5. Intervention Delivery Mode and Duration



[a]Time Length Not Specified in 2 Interventions

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

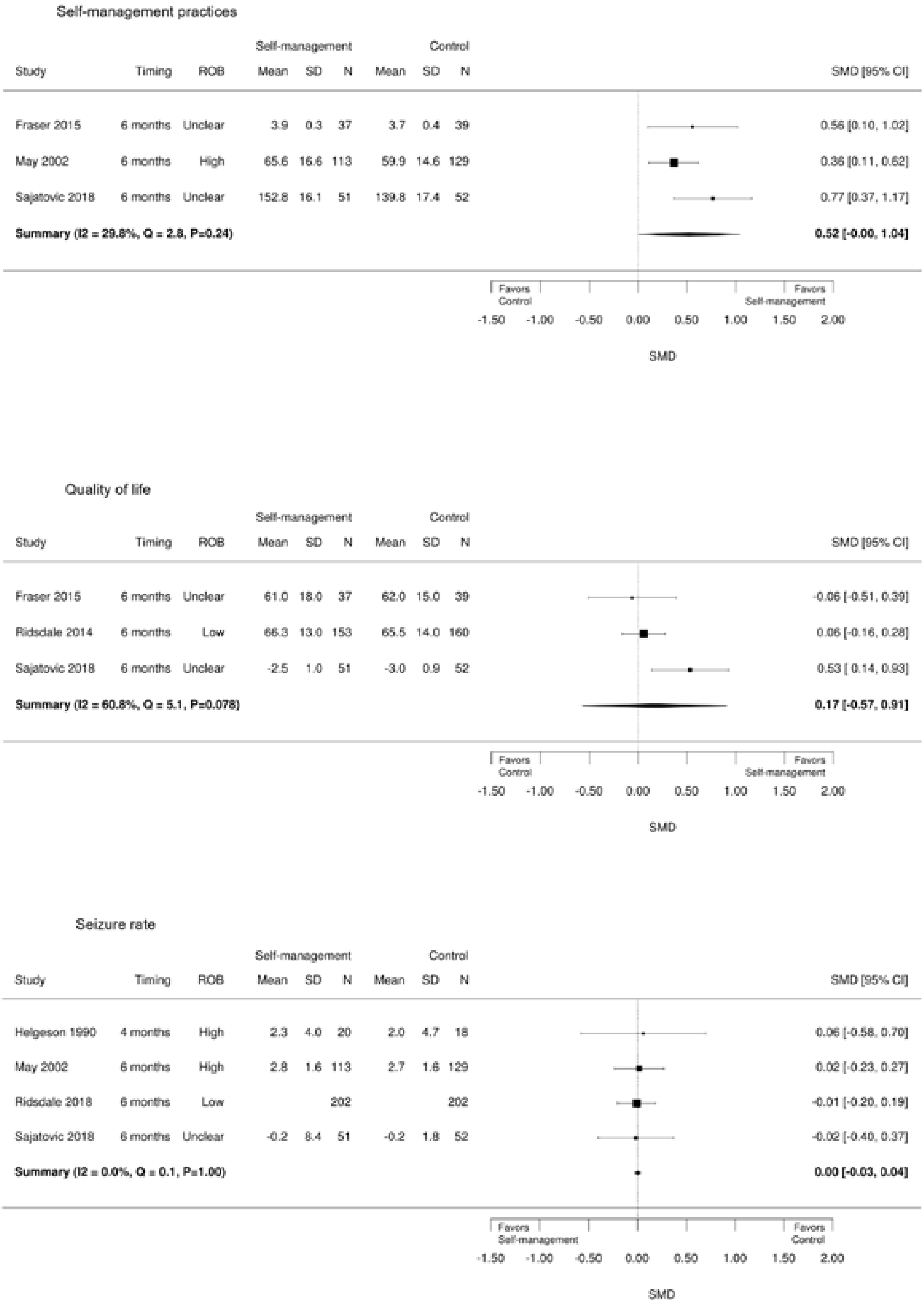
Four randomized studies and 1 nonrandomized study reported effects on QOL using the 10- or 31-item versions of Quality of Life in Epilepsy Inventory (QOLIE). The QOLIE overall score is calculated as a weighted average of 7 multi-item subscales and standardized to a 0-100 point total score; the minimum 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



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 (0 to 1.04 higher)	**Low certainty** of improved self-management (rated down for serious ROB and reporting bias)
Quality of life	4 randomized (492) 1 nonrandomized (747)	SMD 0.17 (0.57 lower to 0.91 higher) MD 0.5 (6.4 lower to 7.4 higher)	**Low certainty** for no effect (rated down for inconsistency and imprecision)
Seizure rates	4 randomized (787)	SMD 0.00 (-0.3 lower to 0.04 higher)	**Moderate certainty** for no effect (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.

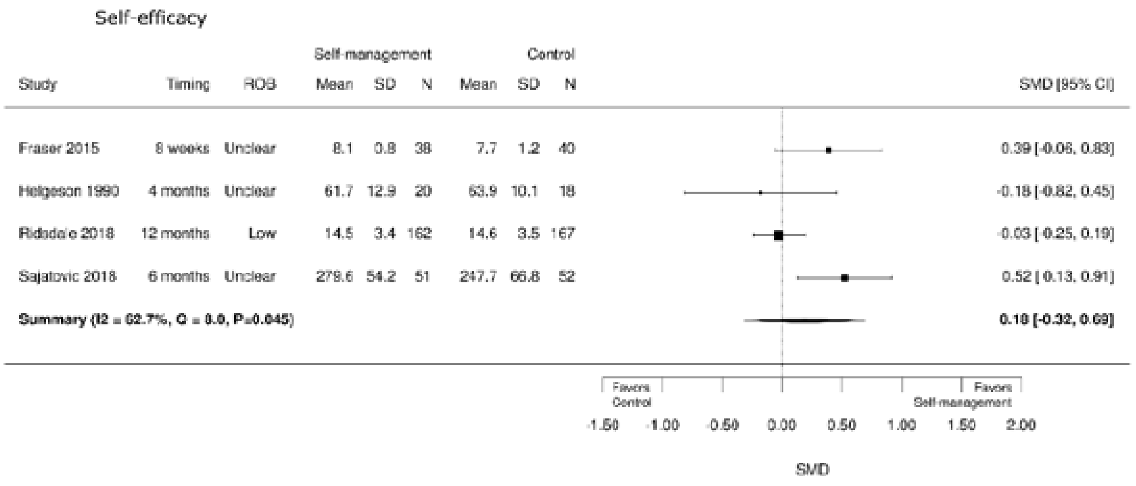
Medication Adherence

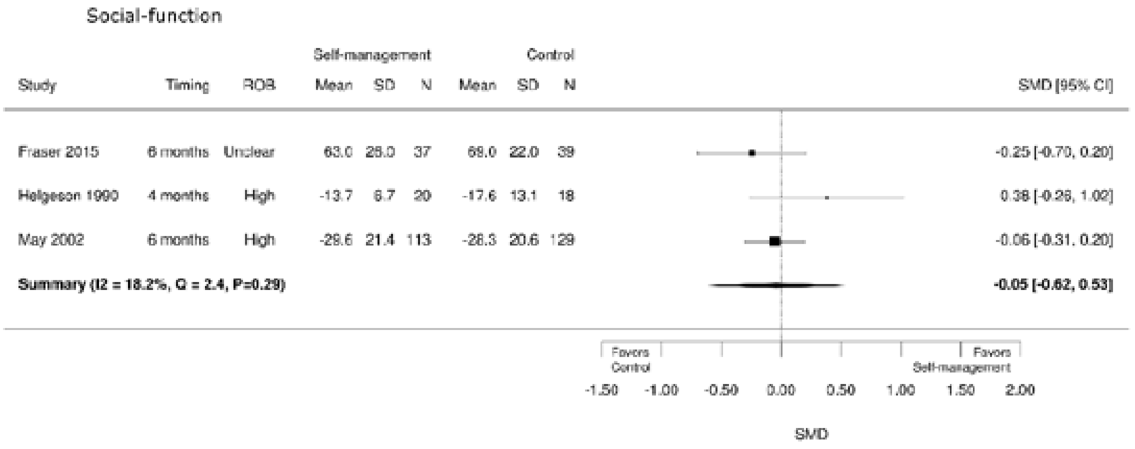
Two educational self-management studies reported effects on medication adherence using self-report measures. Neither a web-based intervention (WebEase),[47] nor an in-person educational intervention (SMILE-UK)[57] improved medication adherence assessed at 6 weeks (SMD 0.05, 95% CI -0.32 to 0.43) and 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.

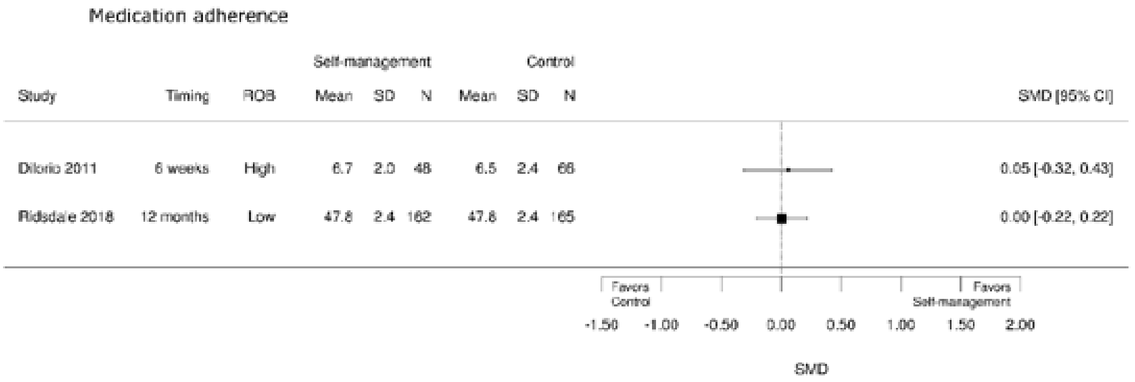
Emergency Department Visits and Safety

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







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

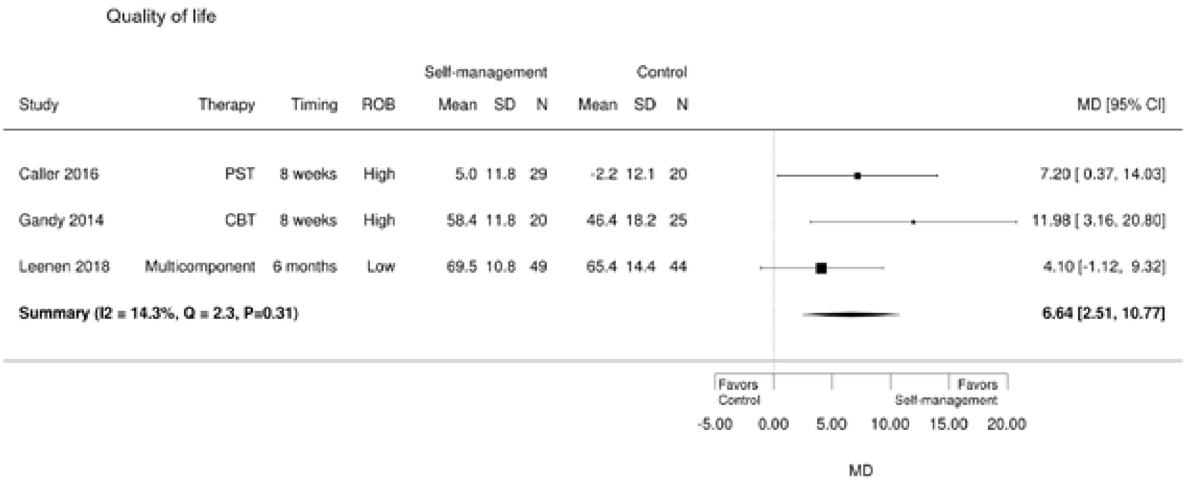
Three studies reported the effects of psychosocial therapy interventions on QOL; all measured QOL with the QOLIE. Studies evaluated problem-solving therapy with or without cognitive training,[46] CBT,[49] and a multicomponent self-management intervention (ZMILE) with an emphasis on self-management skills 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]

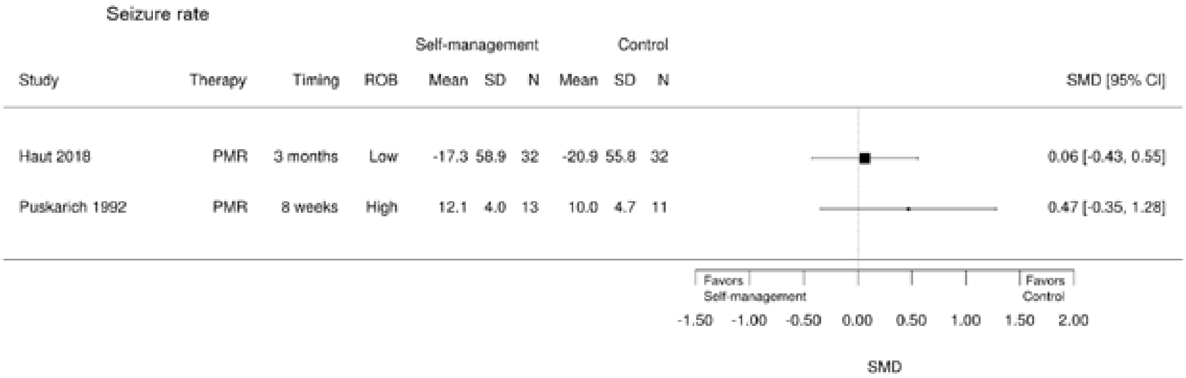
An additional small randomized study compared CBT with a relaxation therapy control.[54] We considered the relaxation arm an active intervention. The study, with unclear ROB, reported a significant improvement in seizure control in the CBT group versus relaxation control (Cohen's D 0.63; p <0.01), and 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 (2.51 to 10.77 higher)	**Low certainty** for improved quality of life (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 (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.

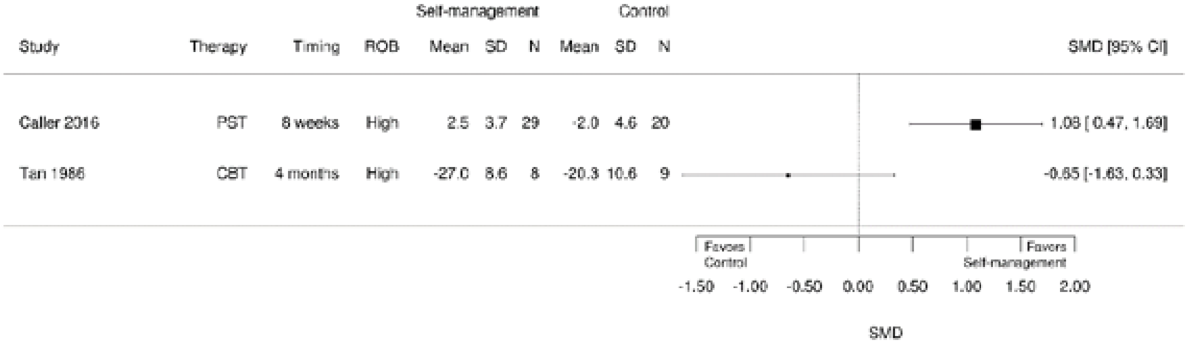
Social Function

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



Study	Therapy	Timing	ROB	Self-management Mean	Self-management SD	Self-management N	Control Mean	Control SD	Control N	SMD [95% CI]
Caller 2016	PST	8 weeks	High	2.5	3.7	29	-2.0	4.6	20	1.08 [0.47, 1.69]
Tan 1986	CBT	4 months	High	-27.0	8.6	8	-20.3	10.6	9	-0.65 [-1.63, 0.33]

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

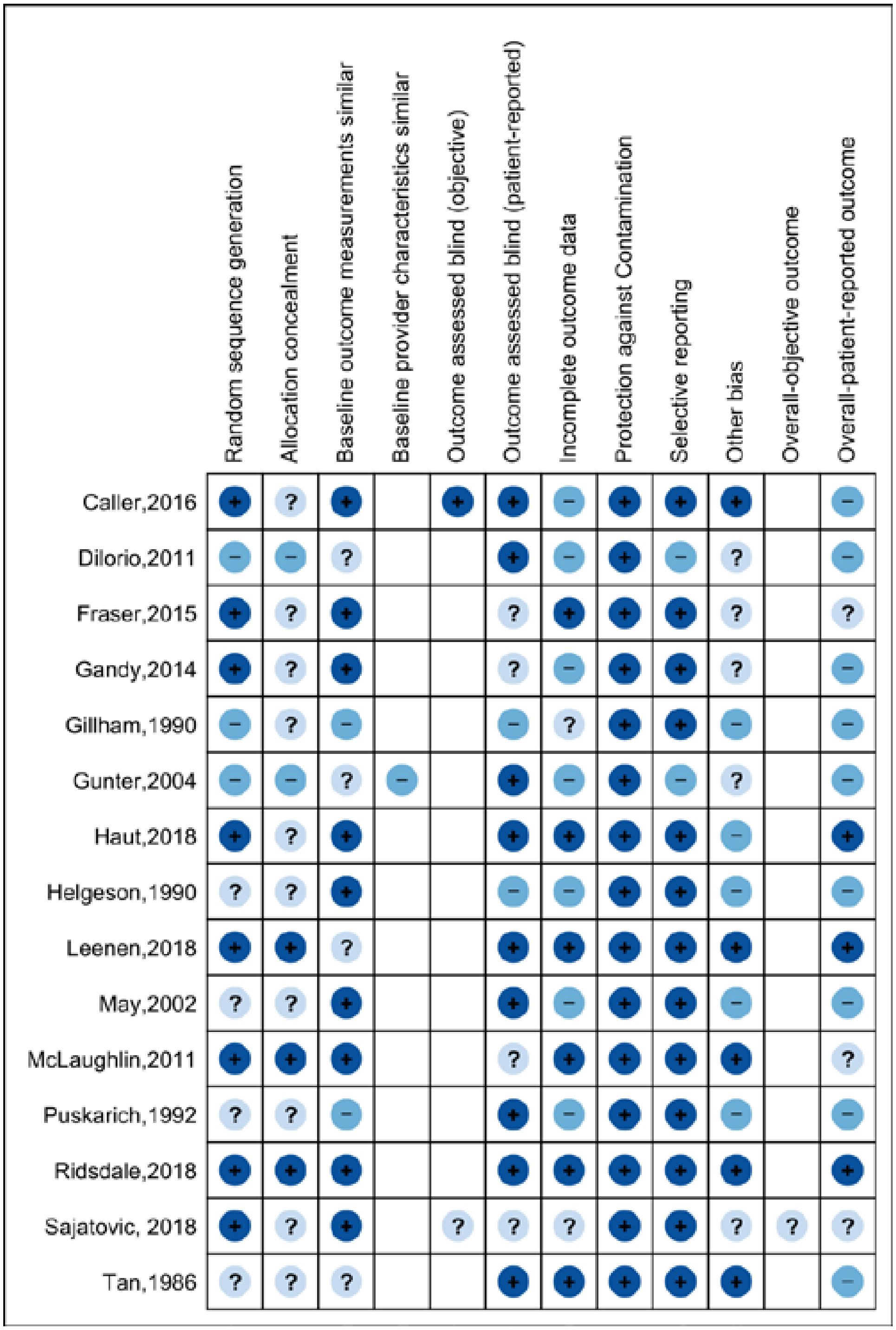
Effects of Interventions on Other Outcomes

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.

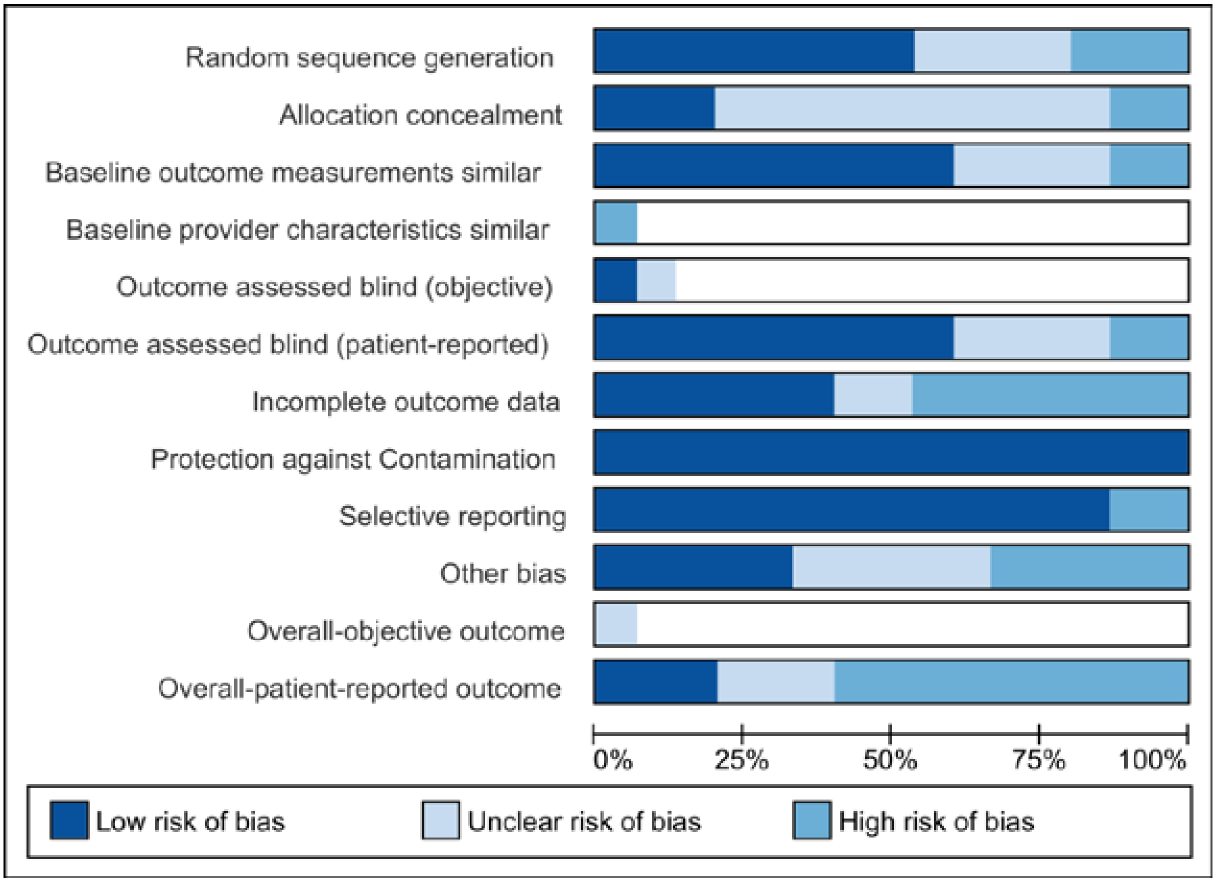
Figure 10. Risk of Bias Ratings for the Included Studies[a]



	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]

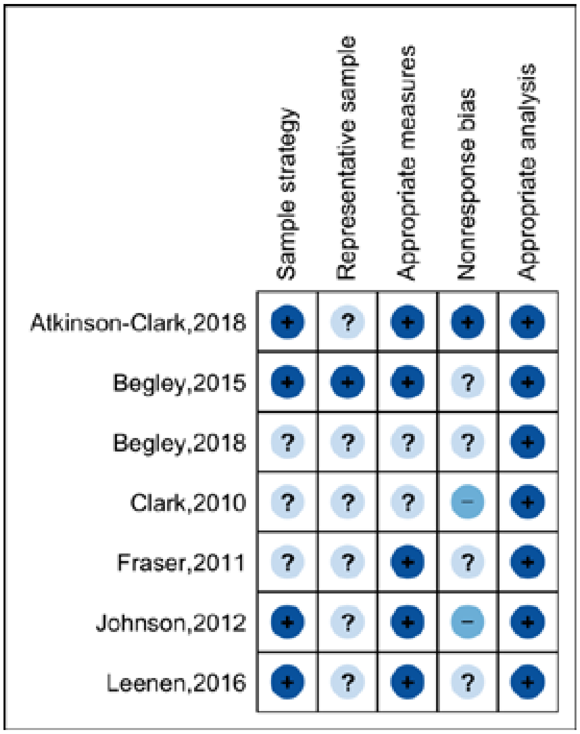
Clinician Interventionist

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]

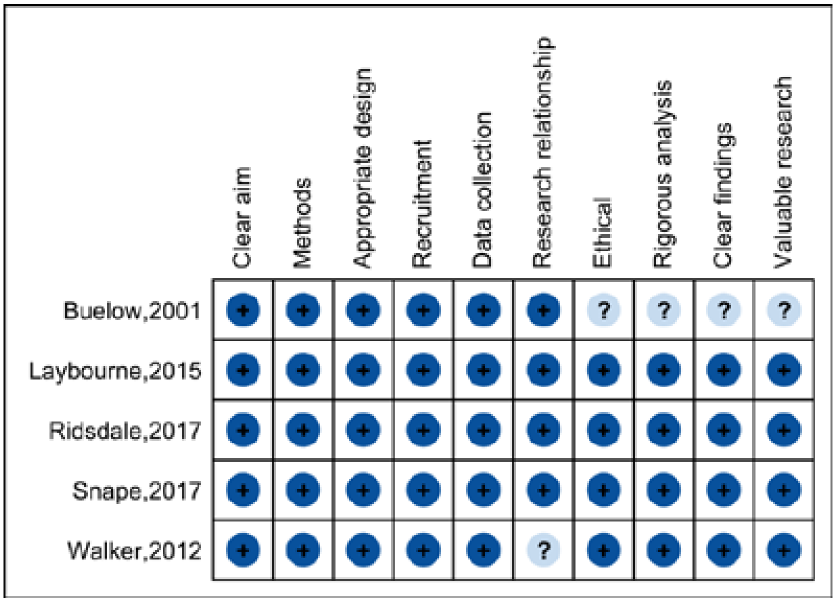


	Sample strategy	Representative sample	Appropriate measures	Nonresponse bias	Appropriate analysis
Atkinson-Clark,2018	+	?	+	+	+
Begley,2015	+	+	+	?	+
Begley,2018	?	?	?	?	+
Clark,2010	?	?	?	−	+
Fraser,2011	?	?	+	?	+
Johnson,2012	+	?	+	−	+
Leenen,2016	+	?	+	?	+

[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]

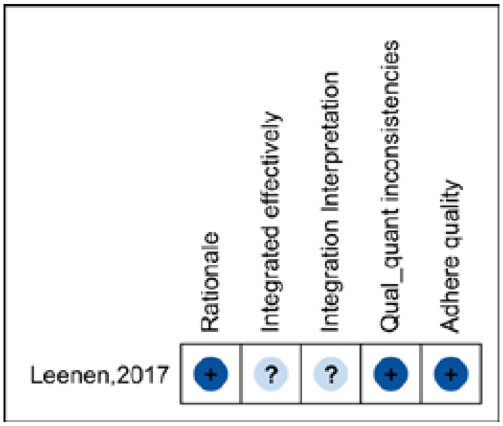


	Clear aim	Methods	Appropriate design	Recruitment	Data collection	Research relationship	Ethical	Rigorous analysis	Clear findings	Valuable research
Buelow,2001	+	+	+	+	+	+	?	?	?	?
Laybourne,2015	+	+	+	+	+	+	+	+	+	+
Ridsdale,2017	+	+	+	+	+	+	+	+	+	+
Snape,2017	+	+	+	+	+	+	+	+	+	+
Walker,2012	+	+	+	+	+	?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

[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. · 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). · 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. · Research is needed on outcomes most valued by patients with epilepsy, and how to best measure these outcomes. · 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.

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