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Self-management for Adults with Epilepsy: Aggregate Managing Epilepsy Well Network Findings on Depressive Symptoms

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Abstract

Objective: To assess depressive symptom outcomes in a pooled sample of epilepsy self-management randomized controlled trials (RCTs) from the Managing Epilepsy Well (MEW) Network integrated research database (MEW DB).

Study Design and Setting (Methods): Five prospective RCTs involving 453 adults with epilepsy compared self-management intervention (n=232) vs. treatment as usual or wait-list control outcomes (n=221). Depression was assessed with the 9-item Patient Health Questionnaire (PHQ-9). Other variables included age, gender, race, ethnicity, education, income, marital status, seizure frequency and quality of life. Follow-up assessments were collapsed into a visit 2 and a visit 3; these were conducted post-baseline.

Results: Mean age was 43.5 (SD 12.6), nearly 2/3 women and nearly 1/3 African-American. Baseline sample characteristics were mostly similar in the self-management intervention group vs. controls. At follow-up the self-management group had a significantly greater reduction in depression compared to controls at visit 2 (P <.0001) and visit 3 (P=.0002). Quality of life also significantly improved in self-management group at visit 2 (P=.001) and 3 (P=.005).

Conclusions: Aggregate MEW DB analysis of five RCTs found depressive symptom severity and quality of life significantly improved in individuals randomized to self-management intervention vs. controls. Evidence-based epilepsy self-management programs should be made more broadly available in neurology practices.

Keywords

epilepsy; seizures; self-management; depression; quality of life

Introduction

Epilepsy self-management is an approach that helps people with epilepsy learn skills to help them better manage their epilepsy and its effect on daily life. Three broad areas targeted are treatment management, seizure management, and life-style management.[1–8] In 2007, the US Centers for Disease Control and Prevention (CDC) established the Prevention Research Centers' Managing Epilepsy Well (MEW) Network to develop, test, and disseminate epilepsy self-management interventions.[3,9]

The MEW Network has developed an integrated database (MEW DB) that pools data from epilepsy self-management studies to conduct aggregate and secondary analysis.[10,11] A recent analysis from the MEW DB that examined correlates of depressive symptoms assessed with the 9-item Patient Health Questionnaire (PHQ-9) found more severe depression in those with poorly controlled seizures.[12] Other studies demonstrate that depression in epilepsy is common and associated with powerful negative effects including worse seizure control, poor quality of life, and premature mortality due to suicide.[13–15]

A recent literature review of psychological treatments in people with epilepsy found that one third of patients receiving cognitive behavioral therapy (CBT) interventions, compared to 10% of controls, could be considered "reliably improved".[16] However, given the great number of undertreated people with epilepsy who also have depression, the development of additional psychological approaches, including alternatives to CBT, is warranted. There is considerable conceptual overlap among psychological approaches intended to help improve health outcomes among people with epilepsy. For example, both CBT and epilepsy self-management interventions include a focus on improving emotional regulation and the development of personal coping strategies that address solving current problems.[16,17] While there is still a relative paucity of randomized controlled trials (RCTs) focused on epilepsy self-management interventions,[18] the CDC-supported MEW Network website describes evidence-based epilepsy self-management intervention such as Home-Based Self-management and Cognitive Training Changes lives (HOBSCOTCH) approach intended to improve cognitive problems in adults with epilepsy and the Targeted Self-Management for Epilepsy and Mental Illness (TIME) approach targeted to adults with epilepsy and comorbid mental health conditions as well as emerging research for self-management interventions that are still in development.[19] Given the MEW Network's focus on depression comorbidity, a number of sites conducting RCTs in epilepsy self-management interventions have the PHQ-9 as a primary or secondary outcome. All MEW Network RCTs have used a treatment as usual or wait-list comparison control, providing relative homogeneity in study design.

Given the critical need for managing depressive symptoms in epilepsy and the limited benefit with standardized psychological approaches such as CBT[17] this aggregate analysis was conducted to address the broad question of whether a curriculum-driven epilepsy self-management intervention can improve depression outcomes in people with epilepsy. This is a first-ever evaluation of the MEW DB longitudinal data to examine depressive symptom severity outcomes in a pooled sample of epilepsy self-management intervention RCTs. We hypothesized that individuals randomized to a self-management intervention would have greater reduction in depressive symptom severity over time compared to controls.

Methods

Overview:

This analysis of longitudinal data included 453 adults with epilepsy enrolled in five MEW Network prospective randomized controlled epilepsy self-management intervention trials. Details describing the MEW Network, including data harmonization, have been described elsewhere.[9] The aggregate data was derived from individual MEW Network research studies with approval by the Institutional Review Board of University Hospitals Cleveland Medical

Center. Only RCTs that included use of the PHQ-9 administered in a longitudinal manner were included in this analysis. The de-identified data used for the analysis were obtained from the HOBSCOTCH trial at Dartmouth-Hitchcock Medical Center,[5] the PACES (Program of Active Consumer Engagement in Self-Management) trial from the University of Washington, the FOCUS (Figure out the problem, Observe your routine, Connect your observations and choose a change goal, Undertake a change strategy, and Study the results) trial from the University of Michigan, and the TIME and SMART (Self-management for people with epilepsy and a history of negative health events) trials from Case Western Reserve University. All RCT participants were adults at least 18 years of age or older. All studies had a self-reported diagnosis of epilepsy except where noted in the specific study descriptions below. None of the studies required a depression diagnosis or a specific depression severity threshold for study inclusion. All study participants expressed informed consent for participation in the respective studies.

Description of each study

HOBSCOTCH [5]: Study design: Prospective RCT

Inclusion criteria: Adult patients with a diagnosis of epilepsy (confirmed by clinical evidence or ancillary studies). Epilepsy was controlled or uncontrolled but without severe intellectual disability. Participants had subjective memory complaints defined as scores of ≤ 7 on a subset of cognition questions of the Quality of Life in Epilepsy (QOLIE-31). (Subset questions were normalized to a score between 0 and 10.)

Sample: 66 adults, age 18–65 years

Description of the intervention: Self-management intervention delivered one-on-one, primarily over the phone. Combines problem-solving therapy with memory strategies.[20]

Intervention comparator: 24-week wait-list control

Key outcomes: Quality of life and objective memory. Depressive symptom severity using the PHQ-9 was assessed as a co-variate. In the original study primary outcome report, depression scores among the treatment cohorts showed improvement but did not reach statistical significance.[5]

Total study duration, timing of research assessments: 24 week study, assessments at baseline, 8–10 weeks (visit 2) and 24 weeks (visit 3).

PACES[6]: Study design: Prospective RCT

Inclusion criteria: Epilepsy without substantive cognitive impairment. Inclusion criteria also included having active (seizure within the past 6 months) and chronic (at least 6 months since diagnosis) epilepsy.

Sample: 283 adults, age ≥ 18 years

Description of the intervention: In-person, 8-week medical and psychosocial self-management group intervention that is focused on improving medical and psychosocial management, problem-solving, and behavioral activation.

Intervention comparator: treatment as usual.

Key outcomes: The primary study outcomes were epilepsy self-efficacy, epilepsy self-management, and goal attainment. Depression (PHQ-9) was assessed as a secondary outcome. In the original study primary outcome report, depressive symptoms were significantly improved at program completion.[6]

Total study duration, timing of research assessments: 24-week study. Research assessments were conducted at baseline (start of program), immediately post-intervention (8 weeks/visit 2), and at 24 weeks post-program (visit 3).

FOCUS: Study design: Prospective RCT. Study outcomes have not been published.

Inclusion criteria: Adults with epilepsy for at least one year, taking antiepileptic medication daily and being able to identify a support person willing to participate.

Sample: 130 adults ≥ age 21years

Description of the intervention: 8-week hybrid in-person workshop and telephone coaching program that developed self-regulation skills in both adults with epilepsy and a key friend or family member who provides support.

Intervention comparator: Control group members received written patient education materials on topics known to impact quality of life for PWE (e.g., sleep and stress) and information on regional and national epilepsy resources.

Key outcomes: The primary study outcome was the 31-item QOLIE-31. Depression, using the PHQ-9, was assessed as a secondary outcome. In the original study analysis, no significant differences between the intervention and control groups were found in pre-post changes in depression.

Total study duration, timing of research assessments: 40-week study. Research assessments (telephone surveys) were conducted at baseline (prior to start of program) and approximately 40 weeks from baseline. Active intervention period was 10 weeks.

SMART[21]: Study design: Prospective 24-week RCT. The RCT was followed by a 12-month extension follow-up phase.

Inclusion criteria: Epilepsy diagnosis and occurrence of a negative health event (NHE) defined as at least one seizure, emergency room visit, hospitalization or self-harm attempt within the past 6 months.

Sample: 120 adults, age ≥ 18 years

Description of the intervention: Remotely-delivered (web or phone) nurse + peer educator group-format self-management intervention focused on managing seizures, stress and life-style to optimize health functioning.

Intervention comparator: 24-week wait-list control

Key outcomes: The primary study outcome was change in NHE counts from baseline to follow-up assessments at week 12 and week 24. Depression using the PHQ-9 was assessed as a secondary outcome. In the original study primary outcome report, depression scores were significantly improved in SMART vs. controls.[21]

Total study duration, timing of research assessments: Only the 24-week RCT data was used for this analysis. Research assessments done at baseline, 10 weeks (visit 2) and 24 weeks (visit 3).

TIME[7]: Study design: Prospective RCT

Inclusion criteria: Epilepsy and the presence of comorbid serious mental illness defined as schizophrenia, bipolar disorder or major depression. Depressive symptoms not required for inclusion.

Sample size, mean age: 44 adults, age ≥ 18 years

Description of the intervention: In-person, nurse and peer educator lead group-format intervention to improve both mood and epilepsy outcomes.

Intervention comparator: Treatment as usual

Key outcomes: The primary study outcome was depressive symptom severity assessed with the Montgomery Asberg Depression Rating Scale.[22] Depressive symptoms using the PHQ-9 were assessed as a secondary outcome. In the original study primary outcome report, depression scores were significantly improved in TIME vs. controls.[7]

Total study duration, timing of research assessments: 16-week study. Research assessments were conducted at baseline, 12 weeks (visit 2) and 16 weeks (visit 3) follow-up.

Measures:

Variables assessed in the studies included age, gender, race, ethnicity, educational level, income, marital/relationship status, seizure frequency and two standardized measures that evaluated depressive symptom severity and epilepsy-related quality of life.

Depressive symptom severity:

Depressive symptom severity was assessed using the 9-item Patient Health Questionnaire (PHQ-9) a widely used and validated self-rated depression scale.[23] The PHQ-9 incorporates diagnostic and statistical manual (DSM) diagnostic criteria, with scores ranging from 0–27. Items are scored on a 0–3 continuum, with higher scores indicating worse depressive symptom severity. Based on total PHQ-9 scores there are several well-documented groups of

depressive severity: 1–4 Minimal depression, 5–9 Mild depression, 10–14 Moderate depression, 15–19 Moderately severe depression, and 20–27 Severe depression.

Quality of life:

Quality of life was assessed with an adapted version of the 10-item Quality of Life in Epilepsy (QOLIE-10) instrument, a self-administered questionnaire developed from the original QOLIE-89.[24] The QOLIE-10 has good test-retest reliability and correlates well with longer versions of this instrument.[25] A 31-item version of the QOLIE (QOLIE-31) and a patient-weighted version of the QOLIE (QOLIE-P) include the same 10 questions but have slightly different scoring ranges (1–6, 1–4) on three items. Given the slightly different versions of the questions across studies in the MEW DB, scores were calibrated to yield a total possible score range of 1–5, with lower scores indicating better quality of life and fewer problems related to epilepsy.

Data Cleaning and Harmonization:

All MEW-DB data are linked following a study protocol and a data dictionary with labels for each variable. Study datasets were first evaluated to confirm that data dictionary variables clearly delineated dataset content and assessment timing. As has been described elsewhere, data mapping was done to allow integration between study-specific variables and the MEW common terminology system, and involved reconciling differences in both data values as well as interval values used to categorize the data elements.[10] For seizure frequency, we "pro-rated" counts based upon the time interval being assessed to derive a past 30-day seizure frequency. For example, if the original study's seizure count data were derived from a 90-day period, we would divide the count by 3 to calculate a 30-day seizure frequency. For the longitudinal component of the analysis, given that our intent was to evaluate the trajectories of depressive symptom severity over time, we collapsed data-collection follow-up time-points into two groups of follow-up assessments. Visit 2 was the first assessment conducted after completion of the self-management intervention and visit 3 was the second assessment done after the self-management intervention. Thus visit 2 was conducted 8–12 weeks after baseline (except for FOCUS which had a single follow-up visit at 36–40 weeks), while visit 3 was conducted 16–36 weeks after baseline. Since the FOCUS study had only one follow-up assessment, the follow-up visit was considered the visit 2 data collection point.

Data analysis:

Statistical analysis was performed using SAS 9.4 (SAS Institute, NC). Descriptive analyses characterized the baseline sample and examined change over time in PHQ-9. Longitudinal mixed models from baseline to visit 2 and visit 3 were conducted. A Type I error rate of 0.05 was used. To validate the pooled longitudinal PHQ-9 total findings and confirm that they were not contingent upon a single study, a series of t-tests for the change from baseline to visit 2 and change from baseline to visit 3 were conducted by leaving out each one of the studies, one at a time. To examine the relationship between variables at baseline and change in PHQ-9 over time, mixed model analyses were conducted in the combined group of intervention + controls. Given the known relationship between quality of life and depressive

symptom severity, the association between a 1-point change in QOLIE-10 and PHQ-9 was also quantified.

Results

Baseline sample:

Table 1 shows characteristics of all individuals with epilepsy in the pooled sample (N=453), as well as by treatment status; self-management intervention group (N=232) vs. controls (N=221). Mean age of the combined sample was 43.5 years (SD 12.6) with nearly 2/3 being women and nearly 1/3 being African-American (Table 1). While the majority of the combined sample had some education beyond high school (68.6 %, N=308), the majority were living in restricted financial circumstances with 69.6% (N=227) with an annual income below US $25,000. Most demographic and clinical characteristics were similar between intervention and control groups. Only marital status was statistically different between the intervention vs. control groups with slightly more individuals in the intervention group (38%, N=46) vs. controls (21.6%, N=27) being married or partnered.

Change in depressive symptom severity over time:

Tables 2a and 2b show the change over time in total mean PHQ-9 scores in the self-management intervention vs. control groups and in each of the five RCTs separately. As seen in Figure 1, in the pooled sample over the three assessment time-points, individuals randomized to self-management intervention had a significantly greater reduction in total depressive symptom severity compared to controls at visit 2 (P<.0001) and at visit 3 (P=.0002). As noted in Table 3, the validation exercise in which each study was omitted one at a time and the remainder evaluated for change over time showed largely similar findings to the pooled analysis with respect to change in PHQ-9 totals between baseline and visits 2 and 3. In addition to examination of PHQ-9 as a continuous variable we also examined the clinically relevant change in the sample proportion in the self-management intervention group vs. the control group who improved from having a depressive symptom severity score in the moderately depressed (PHQ-9 score of ≥ 10. There was no statistically significant difference in the percent of the intervention group (41.3%) versus control group (44.2%) that had a PHQ-9 score of ≥10 at baseline (P=0.537). However, at visit 3, the percentages were significantly different (P<0.001) with only 24.8% of the intervention group having a PHQ-9 score of ≥ 10 vs. 47.1% of controls.

Association between demographic/clinical variables and change in depressive symptom severity:

As noted in Table 4, quality of life was also significantly improved in self-management intervention vs. controls at visit 2 (P=.001) and visit 3 (P=.005). Mixed-model analyses are shown in Table 5. For the combined sample, treatment assignment, visit time-point, educational level and quality of life at baseline were all significantly associated with change in PHQ-9. Individuals randomized to the intervention had reduced depressive symptom levels over time as evidenced by the significant treatment-time-interaction. Individuals with higher educational levels (at least some college) had lower end-point PHQ-9 scores than those with lower education, with an average difference of 1.87 (SD 0.70). In examining only

the sample of individuals randomized to control, lower education was associated with less improvement in depressive symptoms (P=.033), while educational level was not significantly associated with change in depressive symptoms in the intervention group (data not shown),. The relationship between quality of life and depression was significant, and a 4.9 increase in PHQ-9 (worse depression) corresponded to a 1-point increase in QOLIE-10 (worse quality of life).

Discussion

These analyses, taking advantage of a novel aggregate dataset from a CDC-sponsored research collaborative,[8] investigated the relationship between participation in an epilepsy self-management intervention and depressive symptom severity outcomes over time. Analyses from 5 RCTs that all used a prospective design comparing self-management intervention vs. treatment as usual or waitlist control, suggests that depressive symptom severity is significantly reduced in people with epilepsy who participate in a self-management intervention program. Given the known association of depression with poor outcomes among people with epilepsy,[1–8] the findings have important clinical implications along several dimensions.

A key clinical implication is the potential utility of self-management intervention to advance care for depressed people with epilepsy. A recent literature review[16] found that psychological treatments, which encompass a broad range of non-pharmacological interventions for individuals, families or groups have strong evidence for improving depressive symptoms in epilepsy. However, this review only identified one study that specifically investigated depression outcomes for a self-management intervention.[6] Our analysis provides additional evidence that self-management support can consistently improve depressive symptom severity in epilepsy. In addition to improving depressive outcomes, self-management support in this pooled analysis was associated with improved quality of life for people with epilepsy.

A recent literature review by Luedke and colleagues[17] that specifically evaluated epilepsy self-management interventions suggested that changes in knowledge about epilepsy as well as improvement in self-efficacy, self-management skills, and lifestyle modification might explain, at least in part, the reduction in depressive symptoms that may be observed in people with epilepsy who participate in self-management programs. It is possible that the holistic/whole-person focus, which is an intrinsic element of this approach, can help individuals regulate their emotions and make healthy lifestyle changes that enhance mood and wellbeing. Supportive interactions with self-management interventionists and the group format in some of the programs might also help reduce social isolation and loneliness experienced by some people with epilepsy.

An important feature of the MEW Network applied research agenda is collaboration with community stakeholders, including people with epilepsy, their families, public service agencies, clinicians and healthcare entities to scale-up and disseminate epilepsy self-management approaches.[7,8] Consistent with this science-to-service mission, there are a variety of opportunities for clinicians, patients and families to access MEW Network

programs and tools (https://managingepilepsywell.org/). Another key element of initiating care and support for people with epilepsy who have depression is early screening and identification. The American Academy of Neurology (AAN) includes screening for psychiatric and behavioral disorders at each epilepsy care encounter as a quality measure for the delivery of optimal care and better outcomes for individuals with epilepsy.[26] Effective screening can identify individuals who might benefit from self-management support or other treatments to manage their depression.

An additional clinical implication of our findings relates to the observed trajectory of depression severity in patients with epilepsy who did not receive self-management intervention. In the aggregate data, depression generally did not improve over time. It is possible that the lack of change could have been related to the fact that none of the studies were conducted under blinded conditions and this may have negatively biased outcomes--people who don't expect to get treatment may not get better. However, the extant literature in chronic diseases generally suggests that depression also tends to be chronic for many individuals, especially if untreated.[27,28] Our analysis found that individuals with epilepsy who have less education may be particularly likely to have poor outcomes in the usual treatment/wait-list trajectory; this subgroup might benefit from a more intensive and perhaps less complex form of a self-management intervention. We did not see that baseline level of education was associated with a difference in depression outcomes among individuals randomized to self-management intervention. This might suggest that self-management intervention could, at least in part, level the playing field or minimize health disparities that might otherwise occur among less educated people with epilepsy.

Our results also highlight the close relationship between depressive symptom severity and quality of life (higher/worse depression severity = lower quality of life).[29] The relevance of depressive symptoms to quality of life and other outcomes in people with epilepsy is substantial, and the MEW Network has prioritized a focus on mental health comorbidity with a particular emphasis on depression.[9,30] A non-MEW Network study that analyzed individuals with poorly controlled epilepsy found that in the order of large to small magnitude: depression, low self-mastery, anxiety, stigma, medical and psychiatric comorbidity, poor medication adherence, and more frequent seizures were associated with worse quality of life.[31]

This analysis has a number of limitations including the inherent difficulty in interpreting aggregate outcomes from studies that were conducted in different settings with different eligibility criteria. None of the studies required a depression diagnosis or a specific threshold of depressive symptom severity as part of inclusion criteria and the PHQ-9 is a depression severity instrument that is not specific to epilepsy, in contrast to the epilepsy-specific Neurological Disorders Depression Inventory for Epilepsy (NDDI-E).[32] Calibration needed to harmonize QOLIE data may not have the same validity as the original standardized scale. Studies had follow-up time frequency and durations that were not identical and the process of harmonizing data from visits for the second and 3rd time-point follow-up may have minimized important elements of when depression may or may not change over time in people with epilepsy. The control group in our pooled dataset analysis included individuals with epilepsy who were randomized to treatment as usual and those who were randomized

to wait-list control, which may have introduced variability to the control group. However, strengths of the data include the relatively large sample, representation of minorities and people with frequent seizures, similarity of the demographic and clinical variables among individuals randomized to intervention vs. control, and a validation exercise conducted as part of the analysis. Additionally, the PHQ-9 has been selected as an indicator of depression quality of care by the National Quality Forum[33] and has been widely used in studies of patients with epilepsy.[34]

In conclusion, epilepsy self-management interventions generally addresses a variety of aspects of helping people with epilepsy learn to manage and cope with this common neurological condition. Aggregate randomized controlled trial findings from a national US epilepsy self-management research collaborative suggest that both depressive symptom severity and quality of life improve with epilepsy self-management approaches. Making self-management interventions more broadly available to people with epilepsy who have depression could potentially improve health generally and minimize the likelihood of complications related to epilepsy.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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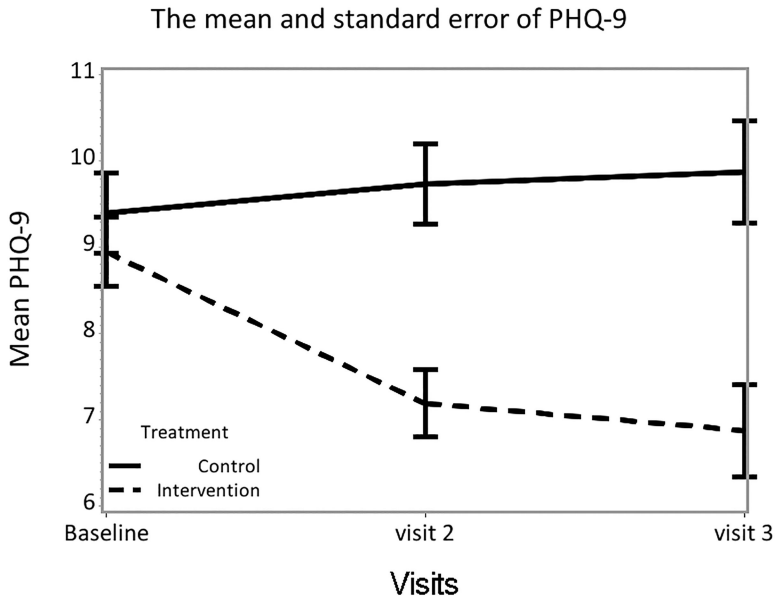

Figure 1:

Total mean score on PHQ-9 over time in self-management randomized participants vs. controls. * P-value at visit 2 = <.0001, * P-value at visit 3 = .0002

Table 1:

Baseline demographic and clinical variables among people with epilepsy randomized to self-management intervention compared to controls

Variable	Total sample N=453	Intervention Sample N=232	Control Sample N= 221	P-value
Age - Mean(SD)	43.5 (12.6)	44.5 (12.5)	42.4 (12.6)	.0662[a]
Female-N (%)	288 (63.7%)	147 (63.6%)	141 (63.8%)	.5893[b]
Race-N (%)				.6434[b]
White	232 (59.9%)	110 (58.5%)	122 (61.3%)	
Black/African American	123 (31.8%)	60 (31.9%)	63 (31.7%)	
Other	32 (8.3%)	18 (9.6%)	14 (7%)	
Ethnicity — N (%)				.5530[b]
Not Hispanic	356 (92.7%)	170 (91.9%)	186 (93.5%)	
Hispanic	28 (7.3%)	15 (8.1%)	13 (6.5%)	
Education — N (%)				.8250[b]
High school or less	141 (31.4%)	73 (31.9%)	68 (30.9%)	
At least some college	308 (68.6%)	156 (68.1%)	152 (69.1%)	
Income — N (%)				.8273[b]
<$25K	227 (69.6%)	114(70.8)	113(68.5)	
$25–50K	40 (12.3%)	20 (12.4)	20 (12.1)	
>$50K	59 (18.1%)	27 (16.8)	32 (19.4)	
Marital status — N (%)				.0048[b]
Married or partnered	73 (29.7%)	46 (38.0)	27 (21.6)	
Other	173 (70.3%)	75(62.0)	98(78.4)	
30-day seizure frequency — Mean (SD)	4.5 (21.0)	4.4 (24.3)	4.5 (16.8)	.4576[c]
QOLIE-10 — Mean (SD)	2.9 (0.9)	2.9 (0.9)	2.8 (0.8)	.6255[a]
PHQ-9 — Mean (SD)	9.2 (6.5)	8.9 (6)	9.4 (6.9)	.4635[a]

[a]: t-test

[b]: Chi-Square

[c]: Mann-Whitney U test

[d]: ANOVA test

[e]: Fisher's exact test

[f]: Kruskal-Wallis test.

QOLIE-10: 10-item Qualify of Life in Epilepsy

PHQ-9: 9-item Patient Health Questionnaire

Table 2a:

Change in PHQ-9 total score over time in people with epilepsy randomized to self-management vs. controls

		Treatment Assignment		
		Intervention	Control	
Visit	Mean (SD)	Mean (SD)	Mean (SD)	P-value
Baseline (N= 453)	9.2 (6.5)	8.9 (6)	9.4 (6.9)	.4635
visit 2 (N=398)	8.5 (6.1)	7.2 (5.4)	9.7 (6.5)	<.0001
visit 3 (N=255)	8.3 (6.5)	6.9 (6.1)	9.9 (6.6)	.0002

Table 2b:

Change in PHQ-9 total scores over time in 5 epilepsy self-management randomized controlled trials

			Treatment Assignment		p-value *
			Intervention	Control	
Study	**Visit (Week)****	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
FOCUS-RCT	Baseline	7.6 (6.1)	7.8 (5.9)	7.5 (6.4)	
	visit 2 (36–40)	7.0 (5.4)	6.9 (5.7)	7.2 (5.1)	0.4051
HOBSCOTCH	Baseline	9.4 (5.9)	9.6 (5.8)	9.2 (6.3)	
	visit 2 (8–10)	8.8 (5.2)	7.8 (4.4)	10.5 (5.9)	0.3395
	visit 3 (24)	8.1 (5.9)	7.1 (5.4)	9.6 (6.4)	0.1586
PACES	Baseline	8.4 (6.1)	8.2 (5.8)	8.5 (6.3)	
	visit 2 (12)	7.2 (5.4)	5.2 (4)	8.8 (5.9)	0.0125
	visit 3 (36)	7 (6.2)	6.3 (6.8)	7.5 (5.5)	0.8277
SMART	Baseline	10.7 (7.2)	10 (6.6)	11.5 (7.8)	
	visit 2 (12)	10 (7.1)	7.8 (6.2)	11.9 (7.4)	0.0050
	visit 3 (24)	9.1 (7)	7.3 (6.6)	10.8 (7)	0.1080
TIME	Baseline	10.7 (5.5)	9.5 (5.3)	11.9 (5.6)	
	visit 2 (12)	11.2 (5.6)	9.2 (5)	13.2 (5.7)	0.1559
	visit 3 (16)	9.5 (6.4)	6.4 (4.4)	12.9 (6.6)	0.0131

*Change from baseline between intervention group vs. control

**: Visits 2 & 3 were follow-up visits conducted after the completion of the epilepsy self-management program was completed. Visit 2 was conducted 8–12 weeks after baseline for all except FOCUS (which had a single follow-up visit conducted at 36–40 weeks). For all studies except FOCUS, which only had 1 follow-up time-point, visit 3 was conducted 16–36 weeks after baseline.

Table 3:

Validation exercise to examine change over time difference in PHQ-9 total scores after sequential omission of each individual RCT.

			Treatment Assignment		
			Intervention	Control	
Dataset	**Difference variable**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**P-value** [a]
All datasets included	diff baseline vs V2	−0.6 (5)	−1.5 (5)	0.3 (4.9)	0.0003
	diff baseline vs V3	−1.2 (5.8)	−2.1 (5.5)	−0.2 (6)	0.0120
HOBSCOTCH omitted	diff baseline vs V2	−0.7 (5)	−1.7 (5.1)	0.3 (4.8)	0. 0004
	diff baseline vs V3	−1.2 (5.9)	−2.2 (5.7)	−0.4 (6)	0. 0305
FOCUS omitted	diff baseline vs V2	−0.5 (5)	−1.7 (4.8)	0.6 (4.9)	0. 0001
	diff baseline vs V3	−1.2 (5.8)	−2.1 (5.5)	−0.2 (6)	0.0120
TIME omitted	diff baseline vs V2	−0.7 (4.9)	−1.6 (4.9)	0.1 (4.8)	0. 0009
	diff baseline vs V3	−1.3 (5.8)	−2 (5.5)	−0.6 (6)	0. 0824
PACES omitted	diff baseline vs V2	−0.5 (5.3)	−1.4 (5.2)	0.4 (5.2)	0. 0026
	diff baseline vs V3	−1.2 (6.2)	−2.4 (5.7)	0.2 (6.5)	0. 0042
SMART omitted	diff baseline vs V2	−0.4 (4.7)	−1.1 (4.8)	0.3 (4.6)	0. 0157
	diff baseline vs V3	−0.8 (5.2)	−1.7 (5.2)	0 (5.1)	0. 0476

[a]: T-test

Table 4.

QOLIE-10 mean scores over time in people with epilepsy randomized to self-management vs. controls

		Treatment Assignment		
		Intervention	Control	
Visit-N	Mean(SD)	Mean (SD)	Mean (SD)	P-value
Baseline (N=453)	2.9 (0.9)	2.9 (0.9)	2.8 (0.8)	0.6255
visit 2 (N=398)	2.7 (0.8)	2.6 (0.9)	2.9 (0.8)	0.0017
visit 3 (N=255)	2.6 (0.9)	2.5 (0.9)	2.8 (0.8)	.0045

Table 5:

Mixed model analysis of the association of baseline demographic and clinical variables with PHQ-9 total score over time in the combined control + intervention group

Variable effect	Num DF	Den DF	F Value	Pr > F
Treatment	1	247	20.39	<.0001
Visit	2	247	3.83	0.0231
Treatment x visit	2	247	3.05	0.0490
Age	1	247	0.00	0.9784
Gender	2	247	0.16	0.8536
Race	2	247	2.82	0.0613
Ethnicity	1	247	0.07	0.7928
Education	1	247	7.23	0.0076
Income	2	247	0.53	0.5874
Marital status	1	247	0.18	0.6711
Seizure frequency	1	247	1.26	0.2631
QOLIE-10	1	247	157.10	<.0001

Num DF: number of degrees of freedom.

Den DF: denominator of degrees of freedom.

F-value: F statistic associated with the given source.

Pr>F:P-value associated with the F statistic of a given source.