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Epilepsy & Behavior 80 (2018) 259–265

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Effectiveness of a multicomponent self-management intervention for adults with epilepsy (ZMILE study): A randomized controlled trial

Loes A.M. Leenen [a,b,c,*], Ben F.M. Wijnen [a,b], Alfons G.H. Kessels [a], HoiYau Chan [a], Reina J.A. de Kinderen [g], Silvia M.A.A. Evers [a,g], Caroline M. van Heugten [d,f], Marian H.J.M. Majoie [b,c,d,e]

[a] Faculty of Health, Medicine and Life Sciences, Department of Health Services Research, CAPHRI Care and Public Health Institute, Maastricht University, Maastricht, The Netherlands
[b] Department of Research & Development, Academic Centre for Epileptology Kempenhaeghe Maastricht UMC +, The Netherlands
[c] Department of Neurology, Academic Centre for Epileptology Kempenhaeghe Maastricht UMC +, The Netherlands
[d] School for Mental Health and Neuroscience (MHENS), Maastricht University Medical Centre, Maastricht, The Netherlands
[e] School of Health Professions Education, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands
[f] Faculty of Psychology and Neurosciences: Department of Neuropsychology and Psychopharmacology, Maastricht University, Maastricht, The Netherlands
[g] Trimbos Institute, Netherlands Institute of Mental Health and Addiction, Utrecht, The Netherlands

ARTICLE INFO

Article history:
Received 18 December 2017
Revised 15 January 2018
Accepted 17 January 2018
Available online 12 February 2018

Keywords:
Epilepsy
Self-management
Self-efficacy
Goal-setting
Multicomponent intervention
Group intervention
PWE & relative

ABSTRACT

Background: The objective of the ZMILE study was to compare the effectiveness of a multicomponent self-management intervention (MCI) with care as usual (CAU) in adult patients with epilepsy (PWE) over a six-month period.
Methods: Participants (PWE & relative) were randomized into intervention or CAU groups.
Self-report questionnaires were used to measure disease-specific self-efficacy as the primary outcome measure and general self-efficacy, adherence, seizure severity, emotional functioning, quality of life, proactive coping, and side-effects of antiepileptic drugs (AED) as secondary outcome measures. Instruments used at baseline and during a six-month follow-up period were the following: disease-specific self-efficacy (Epilepsy Self-Efficacy Scale [ESES], General Self-Efficacy Scale [GSES]); adherence (Medication Adherence Scale [MARS] and Medication Event Monitoring System [MEMS]); seizure severity (National Hospital Seizure Severity Scale [NHS3]); emotional well-being (Hospital Anxiety and Depression Scale [HADS]); quality of life (Quality of Life in Epilepsy [QOLIE-31P]); proactive coping (Utrecht Proactive Coping Competence [UPCC]); and side-effects of antiepileptic drugs [SIDAED]. Multilevel analyses were performed, and baseline differences were corrected by inclusion of covariates in the analyses.
Results: In total, 102 PWE were included in the study, 52 of whom were in the intervention group. On the SIDAED and on three of the quality of life subscales QOLIE-31P, a significant difference was found ($p < 0.05$) in the intervention group. Self-efficacy, however, showed no significant differences between the MCI and the CAU groups. None of the other outcome measures showed any significant difference between the two groups.
Significance: Although we found no statistically significant difference in the primary outcome measure, disease-specific self-efficacy, this MCI could prove promising, since we found improvement in some domains of quality of life in epilepsy scale and a decrease in AED side-effects in the MCI group compared with the CAU group.

1. Introduction

Having epilepsy is associated with psychological and emotional problems, such as depression and anxiety, which are strongly reflected in a reduced quality of life [1,2]. Unpredictable seizures are likely to influence daily activities (e.g., employment) of PWE [2]. Thus, as well as managing their symptoms, PWE and their relatives [3] must acquire disease-specific knowledge, adhere to treatment and lifestyle regimes, and cope with the psychosocial consequences of the condition [4,5].

Most PWE use antiepileptic drugs (AED), and concordance is of great importance for achieving and maintaining positive seizure control [6]. Concordance refers to the consensual agreement about taking AED that has been established between patient and practitioner [7]. Poor concordance has been shown to be the most important cause of poorly controlled epilepsy [6]; many PWE seem to be unaware of missed drug intake [8]. To improve concordance, some self-management programs focus on the use of e-Health tools (e.g., digital pill dispensers) [9], although this is not very common in PWE [10].

* Corresponding author at: Academic Centre for Epileptology Kempenhaeghe, Sterkselseweg 65, 5591 VE Heeze, P.O. Box 61, 5590 AB Heeze, The Netherlands.
E-mail addresses: leenenl@kempenhaeghe.nl (L.A.M. Leenen), b.wijnen@maastrichtuniversity.nl (B.F.M. Wijnen), fons.kessels@maastrichtuniversity.nl (A.G.H. Kessels), h.chan@maastrichtuniversity.nl (H. Chan), RKinderen@trimbos.nl (R.J.A. de Kinderen), s.evers@maastrichtuniversity.nl (S.M.A.A. Evers), c.vanheugten@maastrichtuniversity.nl (C.M. van Heugten), majoiem@kempenhaeghe.nl (M.H.J.M. Majoie).

https://doi.org/10.1016/j.yebeh.2018.01.019
1525-5050/

One of the options for increasing concordance could be self-management support for PWE (and relatives) using an evidence-based self-management program, which includes goal-setting, problem-solving, symptom management, and shared decision-making [11–13]. The aim of self-management support is to provide education and supportive interventions to increase skills and confidence in managing health-related problems [12]. Self-efficacy (i.e., confidence to behave with the intention of reaching a desired goal) is one of the mechanisms responsible for improvement in health outcomes and quality of life, as demonstrated by those attending self-management programs [4,14,15]. Proactive coping is helpful in dealing with anticipated challenges in order to reach the desired goal [16]. The concept of self-management is complex with many different definitions and conceptualizations and, therefore, many forms of support exist [17]. There is little evidence to prove the effectiveness of self-management programs within the care of PWE [18]. We, therefore, developed a multicomponent intervention (MCI), consisting of a self-management education program with e-Health interventions directed at improving self-efficacy, thus, improving the self-management skills of PWE.

The goal of this study (the ZMILE-study) was to evaluate the clinical effectiveness of the MCI. Our primary expectation was that we would find a higher level of disease-specific self-efficacy in the intervention group compared with those who received CAU. Secondarily, we expected to find higher levels of general self-efficacy, adherence (as a proxy for concordance), and proactive coping. We also expected to find a positive change in seizure severity, emotional functioning, quality of life, and experienced side-effects of AED, these outcome measurements are recommended outcomes in epilepsy research [19].

2. Method

2.1. Design

The ZMILE-study was a randomized controlled trial with two parallel groups in which we evaluated the impact of the MCI in comparison with CAU. The complete study protocol has already been published [20]. In this paper, we report the clinical effectiveness. Outcome measurements were assessed at baseline (BS) and at 3 and 6 months' follow-up (FU3M and FU6M). The primary outcome measure of the study was disease-specific self-efficacy; secondary outcomes measures were the following: general self-efficacy, adherence, seizure severity, emotional functioning, quality of life proactive coping, and side-effects of AED. Instruments used to assess outcome measurements are shown in Table 1. The cost-effectiveness and the process evaluation of the ZMILE-study are reported elsewhere [21,22].

2.2. Participants

Eligible PWE for this study were adults who were 18 years or over, living at home, diagnosed with epilepsy, and using AED; who understood the Dutch language; and who were willing and able to use e-Health devices belonging to the MCI [20]. Excluded were PWE who were not able or willing to function in group activities, or when, based on clinical judgment, it was considered that they would not be able to comprehend topics discussed within the MCI (e.g., PWE with cognitive deficits). Patients were not selected or referred based on a preexisting measure of epilepsy self-management as this was a pragmatic trial and this more closely resembles actual practice.

2.3. Procedure

Between March 2014 and December 2015, the Academic Centre for Epileptology recruited PWE during regular attendances at the neurology clinic, via press releases in national epilepsy magazines (Epilepsie, Transmissie) and via social media (Facebook). All potential candidates were informed about the procedure at an initial meeting with one of the researchers. One week later, PWE who wanted to participate were invited for a second visit, were asked to sign an informed consent form, and were allocated randomly to either the intervention or CAU group.

Baseline measurements (BS) were conducted after randomization. All participants received at baseline the Medication Event Monitoring System (MEMS) and a set of questionnaires. Participants were asked to fill in the questionnaires at home and send them back in a prestamped envelope. Prior to the follow-up visits (FU3M, FU6M), the questionnaires were sent by post so that participants could complete them at home. They were collected during the follow-up visits, and the MEMS was read (i.e., the number of times the container was opened). The procedure was approved by the Ethics Committee of Maastricht University/Hospital Maastricht, The Netherlands; an overview is presented in Fig. 1.

2.4. Randomization

To ensure parallel provision of both groups (intervention & CAU), two equal cohorts of PWEs were needed at the moment of randomization. Patients with epilepsy were assigned to the intervention group or the CAU group by means of block randomization. Instead of the intended blocks of 10 PWE, we also used blocks of six, eight, or ten PWE for practical reasons. An assistant, not involved in the treatment nor in the trial, executed the procedure using a randomization program (www.randomization.com). The randomization scheme was distributed to the researcher in sealed envelopes during the first visit, prior to BS.

Table 1
Overview of measurements per time point.

Outcomes	Instrument	Range poor–good	BS	FU3M	FU6M
Primary outcome measure					
Self-efficacy	Epilepsy Self-efficacy Scale (ESES) [37]	33–330	X	X	X
Secondary outcome measures					
General self-efficacy	Generic Self-efficacy Scale (GSES) [38]	10–40	X	X	X
Adherence	MEMS [39]	NA	X	X	X
Adherence	Medication Adherence Scale (MARS-5) [40]	5–25	X	X	X
Seizure frequency	Questionnaire seizure frequency	–	X	X	X
Seizure severity[a]	National Hospital Seizure Severity Scale (NHS3) [41]	27–1	X	X	X
Emotional functioning	Hospital Anxiety and Depression Scale (HADS) [42]	42–0	X	X	X
	Subscale anxiety	21–0			
	Subscale depression	21–0			
Quality of life	Quality of Life in Epilepsy (QOLIE-31P) [24,43]	0–100	X	X	X
Proactive coping	Utrecht Proactive Coping Competence (UPCC) [44]	21–84	X	X	X
Side-effect[b]	Side-effects of antiepileptic drugs (SIDAED) [45]	138–0	X	X	X

BS = baseline outcome assessments; FU3M & FU6M = follow-up outcome assessments at 3 & 6 months.
[a] If no seizures had occurred in the past year, a score of 0 was allocated.
[b] Only the severity of the side-effects was measured.

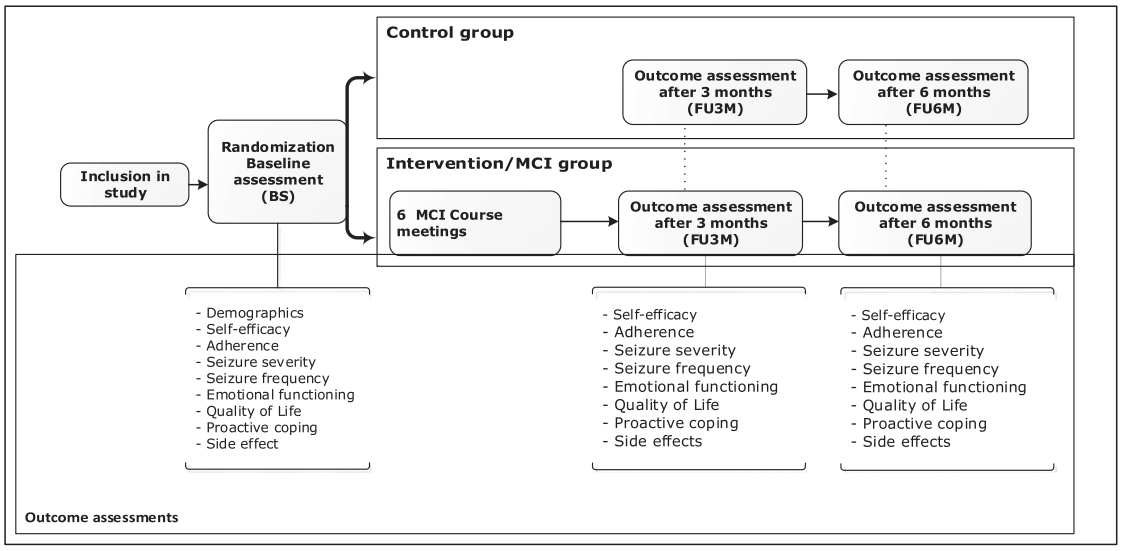

Fig. 1. Overview of the study protocol adapted from Leenen and Wijnen et al. [20]. After 6 months, PWE of the CAU group were also provided the opportunity to receive the MCI outside the study.

2.5. Multicomponent intervention

The MCI consisted of five weekly group sessions of 2 h each, followed by a two-hour booster session after 3 weeks. The groups comprised three to five PWE with possibly a relative, if present and willing to participate. Sessions led by two nurse practitioners were conducted at several locations in the southern part of the Netherlands (Heeze, Maastricht, and Nijmegen). All group sessions consisted of two components: education and practicing goal-setting skills. In the educational part, participants were sharing and discussing strategies about three topics: 1) self-monitoring and self-monitoring using (e-Health) tools; 2) risk-evaluation and management; and 3) shared decision-making/concordance. The goal-setting component of the intervention is based on Aspinwall and Taylors' [16] five stages of proactive coping, namely: resource accumulation; recognition of potential stressors; initial appraisal; preliminary coping efforts; and elicitation and use of feedback concerning initial efforts.

The two e-Health tools used for self-monitoring were a Medication Event Monitoring System (MEMS, Aardex) and a smartphone application 'Eppy' (Epilepsy Foundation, the Netherlands). Medication Event Monitoring Systems are electronic caps with an Liquid Crystal Display (LCD) screen, fitting standard pill bottles, that register the date and time the bottle was opened. These data were stored in an internet-based database end presented in simple plots. Additionally, the LCD-screen provides the user with direct feedback on how many times the bottle had been opened that day. Feedback on medication adherence, as collected by MEMS, was given to the intervention group during the group sessions and after 3 and 6 months' follow-up by a nurse practitioner. 'Eppy' is an application that could be downloaded free to a smartphone, giving PWE the opportunity to keep, for instance, a digital seizure diary or to set reminders for taking medication. Data gathered with the Eppy could be synchronized to a website. Access to this website could be granted to healthcare professionals, by the PWE.

A more detailed description of the intervention has been published previously [20,22].

2.6. Care as usual (CAU)

The control group received unrestricted CAU. Since the ZMILE-study was a pragmatic trial, the CAU-group did not follow a standardized protocol, thus the content of CAU might be variable across PWE, but is expected to be in agreement with standard epilepsy guidelines (http://epilepsie.neurologie.nl). In order to measure adherence, the CAU group also received the MEMS, but without the LCD screen and without the feedback during the visits.

2.7. Outcome measurements

Table 1 presents the questionnaires included in the study. These self-report questionnaires were used to measure disease-specific self-efficacy as the primary outcome measure and general self-efficacy, adherence, seizure severity, emotional functioning, quality of life, proactive coping, and side-effects of AED as secondary outcome measurements. As the MCI was based on a self-management program for patients with type 2 diabetes, which was intended to and shown to significantly improve self-efficacy [23], the Epilepsy Self-Efficacy Scale (ESES) was chosen as primary outcome. At baseline, sociodemographic and a limited number of medical variables, such as year of first seizure, were recorded in a patient-reported questionnaire. More details about the administered measurement can be found in the study protocol [20].

The EuroQol-5D-5L was part of the cost-effectiveness study and, therefore, not included in the present study.

2.8. Sample size & analyses

The required sample size for this study was estimated to be 100 persons (i.e., 50 interventions and 50 CAU) [20].

All statistical procedures were performed using IBM SPSS statistics version 24 for MacOS, and were based on the intention-to-treat principle. The baseline differences between the MCI group and CAU group were analyzed using independent *t*-tests or Pearson's chi-square tests when appropriate. To compare adherence rates, Wilcoxon rank sum tests were used. The first step in handling missing data was to follow the scoring manual of the ESES and HADS questionnaire [24,25], which prescribes using mean values for handling missing data at item level. The SPSS multiple imputations (five times) were used to manage complete data missing from the ESES and HADS, as well as for data missing from other questionnaires.

Multilevel analyses were performed with outcome measurements (BS, FU3M, and FU6M) as within-subjects' factor and group (intervention or CAU) as between subjects' factors to account for the nested structure (e.g., repeated measures) of the data. Baseline differences were

corrected by inclusion of covariates in the analyses. Random intercept was used to account for the difference between PWE. A 2-sided significance level of 0.05 was used [26]. In the analysis of the MEMS, PWE were excluded if they did not initiate their MEMS caps.

3. Results

3.1. Participants

Fig. 2 presents a flowchart showing the path taken by the participants. Overall, 102 PWE took part in the study, of whom 86 completed the trial. All assessments were performed within the schedule of 3 months ± (2 weeks). Although depression is a common comorbidity associated with epilepsy, in this sample, average scores on the HADS did not exceed 6.9 for both anxiety and depression during follow-up. These scores are not above the frequently used cut-off point of 8 to define the presence of depression/anxiety [27]. Table 2 shows the baseline characteristics of the study population.

At baseline, the intervention group had significantly more PWE who were employed (24/50) than the CAU group (11/48) ($p = .02$).

3.2. Clinical effect of the intervention

Table 3 shows the effects of the intervention. At baseline, the ESES scores of the intervention group were significantly higher than that of the CAU group ($p = 0.02$).

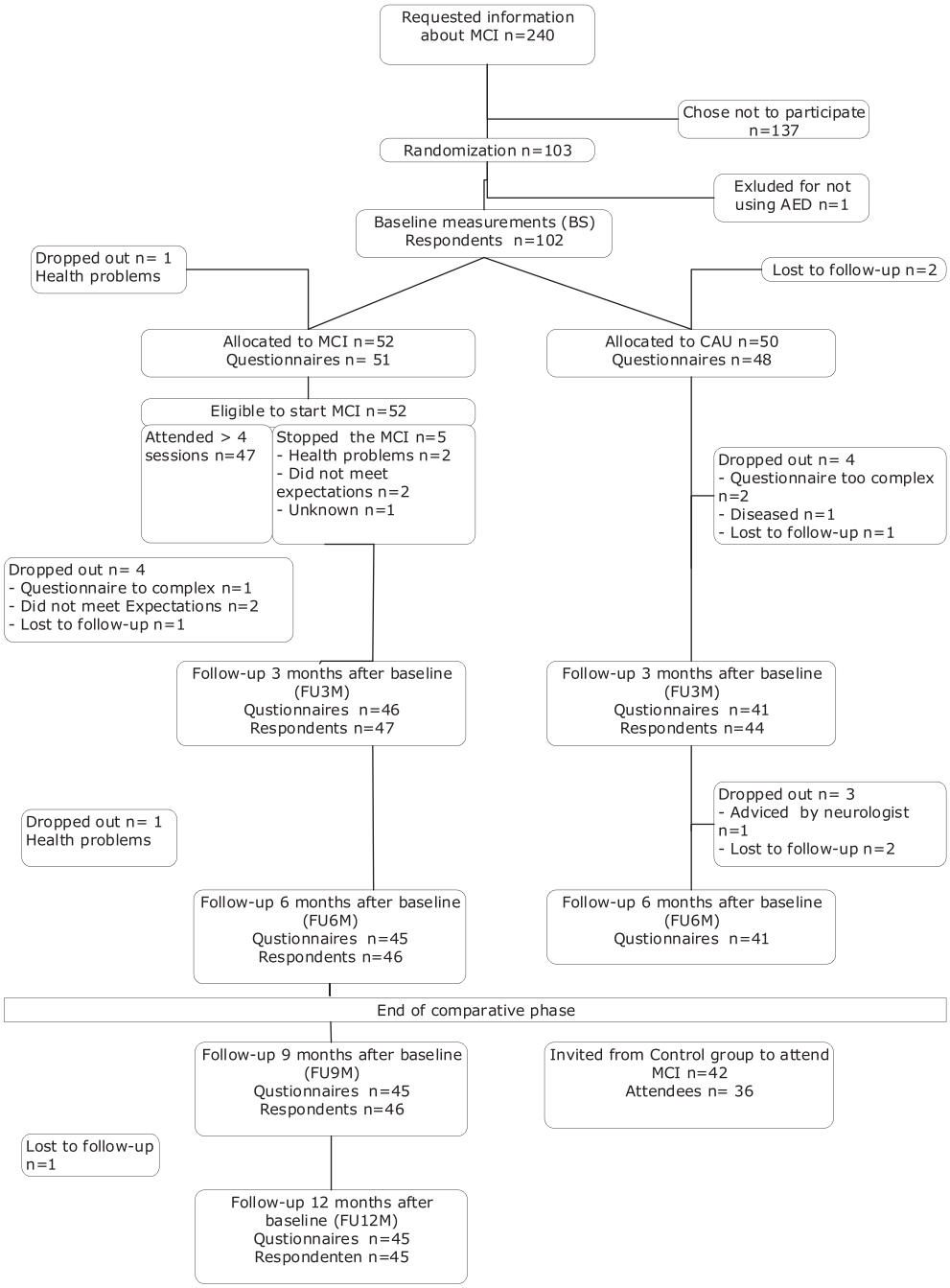

Fig. 2. Flowchart of participants through the study.

Table 2
(Baseline) characteristics of the population.

Characteristics	Intervention group (n = 52)	CAU group (n = 50)	Total (n = 102)
Gender, n (%)			
Male	28 (53.9%)	22 (44.0%)	50(49.0%)
Female	24 (46.2%)	28 (56.0%)	52 (51.0%)
Age in years, mean (SD)	40.0 (13.1)	43.5 (15.4)	41.7 (14.7)
Age group, n (%)			
18–24	7 (13.5%)	7 (14.0%)	14 (13.7%)
25–44	23 (44.2%)	20 (40.0%)	43 (42.2%)
45–64	21 (40.4%)	18 (36.0%)	39 (38.2%)
≥65	1 (1.9%)	5 (10.0%)	6 (5.9%)
Marital status, n (%)			
Married/living with partner	24 (46.1%)	28 (56.0%)	52 (51.0%)
Living alone	15 (28.8%)	11 (22.0%)	26 (25.5%)
Living with parents	7 (13.5%)	8 (16.0%)	15 (14.7%)
Other	3 (5.8%)	1 (2.0%)	4 (3.9%)
Missing values	3(5.8%)	2 (4.0%)	5 (4.9%)
Highest level of education, n (%)			
No education	2 (3.8%)	4 (8.0%)	6 (5.9%)
Primary school	1 (1.9%)	3 (6.0%)	4 (3.9%)
Prevocational secondary school	29 (55.8%)	30 (60.0%)	59 (57.8%)
Secondary school[a]	6 (11.5%)	3 (6.0%)	9 (8.8%)
Higher education[b]	10 (19.2%)	5 (10.0%)	15 (14.7%)
Other	2 (3.8%)	3 (6.0%)	5 (4.9%)
Missing values	2 (3.8%)	2(4%)	4 (3.9%)
Daily life, n (%)			
Study	6 (11.5%)	3 (6.0%)	9 (8.8%)
Work	20 (38.5%)	11 (22.0%)	31 (30.4%)
Entrepreneur	4 (7.7%)	0	4 (3.9%)
Housewife/househusband	3 (5.8%)	5 (10.0%)	8 (7.8%)
Unemployed	9 (17.3%)	7 (14.0%)	16 (15.7%)
Incapacitated	5 (9.6%)	16 (32.0%)	21 (20.6%)
Retirement or early retirement	2 (3.8%)	4 (8.0%)	6 (5.9%)
Other	2 (3.8%)	2 (4.0%)	4 (3.9%)
Missing values	1 (1.9%)	2 (4.0%)	3 (2.9%)
Employment[c]			
Unpaid job/unemployed	27 (51.9%)	36 (72.0%)	63 (61.8%)
Employed	24 (46.2%)	11 (22.0%)	35 (34.3%)
Missing values	1 (1.9%)	3 (6.0%)	4 (3.9%)
Medication at baseline, mean (SD)			
Total number of medications	3.5 (1.7)	4.2 (2.6)	3.8 (2.2)
AED	1.9 (0.9)	2.1 (1.0)	2.1 (1.0)
Missing	3	3	
Seizure frequency at baseline, mean (SD)[d]	4.5 (11.0)	5.8 (11.3)	
Missing	3	4	
Years since first seizure, mean (SD)	20.3 (14.2)	19.9 (15.8)	
Missing	2	7	

[a] Includes: general vocational school, preuniversity school, and secondary vocational education.
[b] Includes: professional and academic higher education.
[c] Sig. difference between groups at 5% level.
[d] Measured as the total seizures in the past 4 weeks before measurement.

The primary outcome disease-specific self-efficacy showed no significant differences between the MCI and CAU group ($p > 0.05$).

Dividing the ESES scores into quartiles (33–107; 108–183; 184–257 and 257–330), we found that most participants gave themselves a score in the third or fourth quartile, i.e., 0/102 in the first, 6/102 in the second, 60/102 in the third, and 36/102 in the fourth quartile.

In total, 49/52 of the intervention and 44/50 of the CAU were included in the analysis. Patients with epilepsy lost to follow-up or who did not use the cap at all, were considered nonadherent. Adherence rates of those included in the MEMS analysis over 6 months were 63.7% for the CAU group and 75.9% for the intervention group; the difference was not significant.

There was a significant difference on the side-effect scale SIDAED ($p = 0.04$), and on three of the subscales of the QOLIE-31P. Subscales 'Emotional wellbeing' ($p = 0.01$), 'Social functioning' ($p = 0.001$), and 'Distress' ($p = 0.01$) had a significantly better result in the intervention group. None of the other outcomes, such as quality of life (QOLIE-31P), adherence (MARS), emotional well-being (HADS), seizure severity (NHS3), and proactive coping (UPCC) showed a significant difference between the two groups.

4. Discussion

The aim of this study was to evaluate the clinical effectiveness of the MCI on disease-specific self-efficacy (primary outcome) and on adherence, seizure severity, side-effects of AED, emotional functioning, proactive coping, and quality of life (secondary outcomes). We found higher levels of disease specific self-efficacy in both groups over time, but no significant differences in disease-specific self-efficacy between the intervention and CAU group. On the secondary outcomes, we found significant differences on side-effects and on some subscales of quality of life, but not on the other outcomes i.e., seizure severity, proactive coping, and depression/anxiety. The significant reduction on drug-related side-effects may be contributed the fact that the MCI focused on patient–physician communication (e.g., How do you prepare a consult?; What do you feel might improve your treatment or what would you like to see changed), which may have led to a more patient-centered AED prescription. However, we have no data available to strengthen this explanation. The significant reduction in subscales of the QOLIE-31P may be explained by the content of the MCI as some of the domains are specifically discussed during the MCI. For example, participants were expected to work on proactive coping and goalsetting which may have impacted the domain "daily activities", "mood", and "distress".

Not finding a significant difference in (disease-specific) self-efficacy is in contrast to other studies on self-management interventions in epilepsy [28] or other chronic conditions [4,11].

In our study, participants showed a high level of disease-specific self-efficacy at baseline. Only 6/102 scored in the bottom half of the scale and 36/102 in the fourth quartile which could reflect a ceiling effect, leaving little room for improvement [29]. The fact that our participants were volunteers, may have contributed to this ceiling effect [30].

Risdale et al. [31] recently found that self-mastery, adherence, depression, and anxiety are all associated with quality of life in PWE. It is possible that self-mastery did not improve in our study, but we did not measure this concept, although we used the same secondary outcomes; i.e., adherence, depression, anxiety, and quality of life [31]. Probably, our understanding of how the different outcomes interact with each other is, at this moment, insufficient.

In addition, we did not assess changes in self-management behavior, such as goal-attainment, so it remains unclear which components contributed to the potential effect of the intervention; this is not uncommon in complex interventions [32]. Furthermore, the CAU was not standardized and there were some additional attributions (i.e., MEMS and visits). This may have diminished the contrast between the interventions and may, therefore, have influenced the study outcomes [33].

Lastly, in our sample, scores on the HADS-A and HADS-D were relatively low (indicating "no cases"). As shown in a recent overview by the Managing Epilepsy Well network, self-management may have an increased potential in patients with epilepsy who are diagnosed as having additional mental complaints such as depression [34].

Strengths of our study were the low drop-out rate and the limited amount of missing data. Data were analyzed using a mixed model, allowing us to impute missing data. Furthermore, the study population was evenly spread over all age groups.

One of the limitations of our study was the fact that the smartphone application 'Eppy' was not maintained and updated and eventually removed from the App Store (Apple Inc., USA and Google Play store, USA) early in 2015. Therefore, only a small group of the participants were able to use the application without experiencing problems with the system. Secondly, in order not to lose interested PWE during certain periods (e.g., holidays) when recruitment rate was low, we started

Table 3
Overview of clinical outcomes and significance testing.

Measures	Intervention group N = 52			Care as usual N = 50)		
	BS	FU3M	FU6M	BS	FU 3 M	FU 6 M
Primary, mean (SD)						
Self-efficacy						
Epilepsy Self-Efficacy Scale	243.8[a] (23.3)	253.2 (30.4)	263.2 (26.3)	230.4[a] (32.3)	244.7 (32.1)	252.3 (32.8)
Secondary, mean (SD)						
Self-efficacy						
General Self-Efficacy Scale	29.4 (5.8)	31.5 (5.2)	31.7 (4.6)	27.9 (5.6)	29.3 (5.1)	30.0 (5.4)
Adherence						
Medication Event monitoring System (MEMS)			75.9% (32.5)			63.7% (36.6)
Medication Adherence Rating Scale (MARS)	23.4 (2.0)	23.6 (1.4)	23.9 (0.9)	23.8 (1.1)	23.9 (1.1)	23.7 (1.3)
Seizure severity						
National Hospital Seizure Severity Scale (NHS3)	6.7 (7.5)	7.3 (8.1)	6.2 (7.3)	9.0 (9.6)	8.4 (9.3)	8.7 (10.0)
Depression/anxiety						
Hospital Anxiety and Depression Scale (HADS) – total	11.3 (6.1)	11.0 (5.2)	9.8 (5.0)	12.7 (5.9)	11.5 (6.2)	11.6 (6.2)
HADS – depression	5.3 (2.6)	5.7 (2.7)	5.2 (2.6)	5.7 (2.3)	5.5 (2.6)	5.5 (2.8)
HADS – anxiety	5.9 (4.3)	5.2 (3.5)	4.7 (3.5)	6.9 (4.3)	6.1 (4.2)	6.0 (4.2)
Quality of life						
Quality of Life in Epilepsy-31 (QOLIE-31P) – total	66.44 (12.3)	69.0 (11.3)	69.5 (10.8)	62.9 (12.4)	62.4 (14.8)	65.4 (14.4)
Subscales						
QOLIE-31P – energy	41.4 (23.8)	46.3 (23.4)	47.8 (22.0)	37.8 (22.1)	42.1 (26.1)	40.2 (23.7)
QOLIE-31P – mood[a]	51.7 (23.8)	53.7 (28.4)	62.0 (23.1)	45.4 (25.5)	47.8 (29.5)	49.0 (27.9)
QOLIE-31P – daily activities[a]	39.1 (26.9)	49.1 (27.4)	55.5 (29.1)	36.4 (25.1)	40.2 (26.7)	39.7 (25.9)
QOLIE-31P – cognition	35.4 (23.9)	50.2 (27.6)	44.8 (23.6)	32.0 (28.0)	36.5 (30.2)	39.7 (25.9)
QOLIE-31P – medication effects	51.6 (30.6)	56.4 (25.7)	57.9 (27.6)	43.2 (27.2)	51.9 (29.0)	45.2 (25.2)
QOLIE-31P – seizure worry	47.5 (31.2)	54.0 (28.3)	53.9 (26.4)	39.3 (26.8)	43.9 (29.8)	42.8 (32.7)
QOLIE-31P – overall quality of life	51.1 (22.8)	54.4 (24.3)	58.8 (22.4)	44.8 (23.2)	48.0 (27.7)	46.7 (27.2)
QOLIE-31P – distress[a,b]	462.8 (128.9)	510.4 (129.9)	534.6 (101.6)	423.7 (142.2)	457.1 (148.9)	442.9 (156.0)
Proactive coping						
Utrecht Proactive Coping Competence (UPCC)	62.6 (11.1)	62.5 (8.5)	64.0 (9.0)	59.7 (6.7)	60.3 (7.9)	61.1 (7.5)
Side-effects						
Side-effects of antiepileptic drugs (SIDAED)[a]	26.9 (21.6)	23.1 (18.7)	19.1 (15.3)	27.1 (20.3)	26.2 (17.6)	25.5 (19.1)

BS = baseline outcome assessments; FU3M & FU6M = follow-up outcome assessments at 3 and 6 months.
[a] Significant at 5% level.
[b] Distress scores are expressed on a scale from 0 to 100 (percentages) for every subscale and are used to weight total (sub)scores.

block randomization at a minimum of six PWE; this was a deviation from the protocol.

Finally, our sample size was based on a standard deviation of 7 points on the ESES. In this study, we found a standard deviation of >30 points. The decrease in study power might have resulted in failure to detect statistically significant findings.

We acknowledge that further research is necessary to establish the overall effectiveness of the MCI. This should take its place alongside process evaluation and economic evaluation of the intervention, both of which showed more favorable outcomes [21,22]. The neurologists who recruited participants believed the intervention to be fruitful for both PWE and neurologist: the former showing more confidence and being prepared, and the latter experiencing a more effective consultation time; this was, however, not measured in this study.

A recently developed instrument for measuring the effectiveness of self-management interventions in epilepsy, the Adult Epilepsy Self-Management Measurement Instrument (AESMMI), may prove to be a great addition to future research. The AESMMI provides an overall effectiveness measure for self-management interventions in epilepsy [35] and is a synthesis of 11 instruments, including the ESES and the QOLIE-31P.

We did not measure mastery, a concept that one can control options/events in life [36]. Mastery experiences are the most effective way of becoming more self-efficacious [14] and are associated with quality of life and emotional functioning [31]. Hence, this would seem to be an important concept to measure in future research.

In conclusion, in spite of the lack of evidence that the MCI is effective looking at self-efficacy, we consider the MCI to be a promising intervention, because of the reduction of side-effects and on improving quality of life on subscales. Further research is needed, but we believe it should be carried out alongside implementation in order to reach a larger group of PWE. We recommend focusing on mastery and the domains of self-management as measured with the AESMMI, as they include most of the well-established outcome measures in epilepsy research (i.e., quality of life, adherence, side-effects, emotional functioning).

Competing interests

The authors declare that they have no competing interests.

Acknowledgments

We would like to thank Our Advisory board for their contribution to the study: Drs. C. Caron (The Netherlands Epilepsy Foundation; Epilepsie Vereniging Nederland; EVN), M.K.H. van Kan-Sieswerda (EVN), Dr. R.H.C. Lazeron (Kempenhaeghe), Drs. I.Y. Tan (Kempenhaeghe), Drs. C.I. Vader (Kempenhaeghe), Dr. A. Pieron (UCB Pharma), Dr. L. Hageman (UCB Pharma), Drs. A. Lenssen (CZ Health Insurance; Centraal Ziekenfonds), and Dr. B. Vrijens (AARDEX Ltd.). Furthermore, we would like to thank Mrs. Vollers for correcting grammatical and spelling errors, Mrs. J. Lambermont for editing the questionnaires.

This study was funded by the Netherlands Organization for Health Research and Development (ZonMw), grant application number 836011018. This study is registered with the Dutch Trial Register, part of the Dutch Cochrane Centre (NTR4484), and has been approved by the Ethics Committee of Maastricht University/Hospital Maastricht. The Netherlands

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