Self-Management education for adults with poorly controlled epilepsy [SMILE (UK)]: a randomised controlled trial

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Scientific summary

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Background

Epilepsy is a common chronic neurological disorder affecting approximately 1% of the UK population. With medication, about 60–70% of people with epilepsy (PWE) can live without seizures. For the rest, recurring seizures can have an impact on their social and work life and can lead to injuries, frequent visits to emergency departments (EDs), psychological conditions and an increased risk of death. For this group of PWE, self-management is potentially important to manage epilepsy and the consequences of recurring seizures. Different methods can be used to increase self-management for chronic conditions. For diabetes mellitus, self-management courses are routinely offered free to users in the UK. There is also a course offered for PWE in German-speaking Europe called Modular Service Package for Epilepsy (MOSES). In the context of a trial, those attending that self-management education course had demonstrated increased knowledge of epilepsy and coping with epilepsy, improved seizure control, better antiepileptic drug (AED) tolerance and fewer side effects.

Objectives

We tested a group Self-Management course for adults with poorly controlled epilepsy in the UK [SMILE (UK)]. Specific objectives were as follows.

- adapt MOSES for the UK population
- assess the feasibility of this adapted version of MOSES in the UK in an external pilot qualitative study
- assess the effectiveness of SMILE (UK) in a randomised controlled trial (RCT) with quality of life (QoL) after 12 months as the primary outcome measure
- evaluate the delivery of the intervention by assessing implementation fidelity in the main trial
- evaluate the cost-effectiveness of SMILE (UK)
- conduct a process evaluation of SMILE (UK) exploring participant views.

Methods

The study was a RCT comparing the effects of SMILE (UK) plus treatment as usual (TAU) with TAU alone. At the end of the trial, SMILE (UK) was offered to the TAU group.

The SMILE (UK) consists of a 2-day group learning course, which aims to support people becoming experts in managing their epilepsy. Courses were provided for groups of 8–12 people. Initial piloting of SMILE (UK) was completed with volunteer members from the user group Epilepsy Action, UK. This pilot study also evaluated the views of the volunteers on the course, benefits of the intervention and how it might be improved.

Participants

Trial participants were recruited from epilepsy clinics from eight hospitals in London and south-east England.

Inclusion criteria were adults aged ≥ 16 years with epilepsy who were prescribed AEDs, with two or more seizures in the previous 12 months and able to provide informed consent, participate in the course and complete questionnaires in English. Exclusion criteria included acute symptomatic seizures as a result of acute neurological illness or substance misuse, psychogenic or non-epileptic seizures only, or severe current psychiatric or medical illness.
The recruitment process involved two stages when patients could opt out from further contact, with 3 weeks per opt-out to return the slips. In the first stage, patients received a letter from their neurologist about the study, advising they could opt out from the next stage. For the patients not opting out of the second stage, medical notes were screened by clinic staff to check eligibility. Potentially eligible patients received a letter about the study from their neurologist, advising that a research worker would contact them with more information if they did not opt out by returning a form within 3 weeks. A research worker then contacted patients to explain the study and verify eligibility. If a patient chose to enrol, the research worker met with them face to face to ensure the patient understood the study and then took written informed consent. Only at this stage was the patient considered enrolled in the RCT and then a baseline assessment was done.

Outcome measures
Outcomes and cost-effectiveness were measured by validated self-report questionnaires at pre-randomisation and at 6 months and 12 months post randomisation. The primary outcome was measured using the Quality Of Life In Epilepsy 31-P (QOLIE-31-P) scale. Secondary outcome measures included the Hospital Anxiety and Depression Scale (HADS), seizure frequency, Impact of Epilepsy scale, Medication Adherence scale from the Epilepsy Self-Management Scale, Stigma of Epilepsy scale, Self-Mastery of Epilepsy scale, and medication adverse effects. We measured quality-adjusted life-years (QALYs) [using EuroQol-5 Dimensions, five-level version (EQ-5D-5L)] and health service use using the Client Service Receipt Inventory. Qualitative research conducted during the pilot and main trial evaluated users’ views on barriers to participation, benefits and how the intervention might be improved.

Sample size
Pharmacological interventions for those with poorly controlled epilepsy using the QOLIE-31-P to measure outcome found an effect size of 0.4 to be clinically significant. A total sample size of 320 (randomised 1 : 1) would provide 91% power to detect an effect size of \( d = 0.4 \) using a two-sided analysis of covariance test with significance set at \( p < 0.05 \). This effect size is considered to be 6–7 points on the QOLIE-31-P scale. This would allow for standard error inflation as a result of group effects [SMILE (UK) is a group treatment]. Assuming an average group size of 10 patients and an intragroup correlation between QOLIE-31-P scores of intraclass coefficient of 0.025, we would need 160 patients in the TAU arm and 16 groups of 10 patients in the SMILE (UK) arm. Inflating the sample size to allow for an estimated 25% attrition required an initial sample of 428.

Primary analysis
The primary clinical effectiveness analysis was by the intention-to-treat (ITT) principle to evaluate the effectiveness of SMILE (UK). The intervention under study [SMILE (UK) + TAU] was compared with TAU on the primary outcome (QOLIE-31-P at 12 months) and the secondary outcomes. An analysis was first undertaken to determine whether or not receiving the full intervention was predictive of missing primary outcome data. As this was found to be the case, multivariate imputation by chained equations (MICE) was used to produce inferences that are valid under such a missing at random data-generating process. The analysis model was a linear mixed-effects model. The random effects were added to account for potential clustering as a result of participants attending the same educational group in the SMILE (UK) arm.

There were seven secondary outcomes that were measured as continuous variables: HADS-anxiety, HADS-depression, self-mastery and control, impact of epilepsy, medication adherence, medication adverse events (AEs), and stigma of epilepsy. All of these were analysed in the same way as QOLIE-31-P (i.e. using MICE followed by a linear mixed-effects model for the respective secondary outcome variable).

Seizure frequency was collected on two different scales: Baker (Baker GA, Jacoby A, Buck D, Stalgis C, Monnet D. Quality of life of people with epilepsy: a European study. Epilepsia 1997;38:353–62) and Thapar [Thapar A, Kerr M, Harold G. Stress, anxiety, depression, and epilepsy: investigating the relationship between psychological factors and seizures. Epilepsy Behav 2009;14(Suppl. 1):134–40]. The seizure frequency variable as measured by the Baker scale was analysed as a binary outcome: less than one seizure per month versus one or more seizure per month. A similar analysis approach was used as above, except
MICE imputed missing outcome values by assuming a logistic regression and a logistic mixed-effects model was used as the analysis model. Similarly, seizure frequency as measured by the Thapar scale was analysed as an ordered categorical outcome: 0–3 seizures, 4–6 seizures, 7–9 seizures or ≥ 10 seizures. The MICE and mixed-effects models used ordinal logistic regression.

Additional analyses
An analysis of baseline data was carried out to better describe the group recruited. In addition, we assessed which clinical, psychosocial and secondary outcome measures were associated with the primary outcome, QOLIE-31-P. This was done using using univariate regressions. When comparing categorical values, predicted means of QOLIE-31-P were calculated within each factor to enable comparisons. One category within each factor was used as a reference (‘ref’).

An assessment of implementation fidelity was also done. A novel instrument was developed to measure adherence and competence of SMILE (UK) facilitators.

Cost-effectiveness analyses
The primary perspective of the economic evaluation was the NHS/Personal Social Services perspective. Other resources relevant to a wider societal perspective such as informal care and productivity loss (because of time off work) were included in the secondary analyses (societal perspective). Data were assessed two ways: complete cases (i.e. only including participants completing service use and QoL data) and on an ITT basis (i.e. according to the group to which they were randomised regardless of intervention receipt). Costs and outcomes were compared between the two arms at baseline and the 12-month follow-up. Cost-effectiveness was assessed by combining the costs with data on the primary outcome measure (QOLIE-31-P) at 12 months. Cost–utility was explored by combining total costs with QALYs, derived from EQ-5D-5L data.

Process evaluation
Within 6 months of attending the course, participants were interviewed about their experience of attending SMILE (UK). Face-to-face semistructured interviews were held on topics about the participant’s experience with epilepsy, negative and positive aspects of the course and whether or not they had changed anything in their self-management behaviours. Interviews were audio-recorded and transcribed verbatim. A line-by-line coding approach was undertaken with codes later grouped into broader emerging themes.

Results

Outcome measures
The study included 404 participants, with a mean age of 41.7 years [standard deviation (SD) 14.1 years]; 54.2% were female and 75.2% were white. The group had been diagnosed with epilepsy for a median of 18 years and 45.8% had another medical condition. The mean QOLIE-31-P score for the whole group at baseline was 66.0 (SD 14.2), with 69.3% having ≥ 10 seizures in the previous year. Clinically relevant levels of anxiety symptoms were reported in 53.6% of the group and depression symptoms in 28.0%. Assessment of self-stigma revealed 63.1% of the group felt mild to high levels of stigma because of their epilepsy.

Characteristics associated with lower QoL were being female, having lower qualifications, not being in employment, having a more recent diagnosis of epilepsy and comorbidity, especially a diagnosed psychiatric condition. Secondary outcome measures associated with QOLIE-31-P were HADS-depression, HADS-anxiety, self-stigma, seizure frequency, self-mastery and medication adherence.

In the intervention group, 74% attended at least one session of SMILE (UK) (i.e. one session was defined as one half-day) and 62% attended the 2 full days. Retention rates in the study were high with 331 out of 404 (82%) completing the 12-month follow-up. AEs were reported from 41 participants and none was
found to be related to the intervention. At the 12-month follow-up, there were no significant differences between the SMILE (UK) and TAU group in any of the outcomes measured.

The implementation fidelity analysis revealed that SMILE (UK) was delivered with a high adherence to the prescribed topics with a high level of facilitator competence.

Cost-effectiveness evaluation
Service use was similar between the two groups. At baseline, general practitioners were the most frequently reported contact, with two or three visits in the previous year. At enrolment, about 40% of the group reported attending EDs in the previous year. At the 12-month follow-up, the proportion of patients reporting use of hospital services had reduced for both groups. The percentage of participants who reported informal care was low, but those who did received substantial help from family and friends.

Findings from the complete-case analysis show that SMILE (UK) is cost-saving, but produces fewer QALYs than TAU. Therefore, the intervention could save costs compared with current treatments available but is associated with lower QoL. The associated incremental cost-effectiveness ratio from a NHS and social care perspective is £5548 and this is how much extra it costs for TAU to produce one extra QALY. The probability of SMILE (UK) being cost-effective (compared with TAU) at the £20,000 willingness-to-pay threshold from the NHS perspective is slightly above 40% (for both the complete case and the ITT analyses). However, this probability is somewhat higher (60%) from the societal perspective, at the same threshold.

Process evaluation
The process evaluation with 20 participant interviews revealed that participants felt that they benefited from the course by being in a group with people similar to them. Some met other PWE for the first time. They reported that learning from others and sharing their own experiences helped them to gain confidence to become experts in their condition. However, nearly half reported memory or language problems that they felt may have either reduced their learning or impaired their ability to self-manage in practice. Many said that the knowledge and confidence led them to interact with health-care professionals more efficiently. Over half (60%) of those interviewed said that they were managing their epilepsy differently. Nineteen out of 20 participants would recommend SMILE (UK) to others.

Conclusion
The SMILE (UK) programme is designed to increase knowledge for PWE. It contains topics addressing medical issues, the science behind epilepsy and the social aspects of living with epilepsy. Delivering this in a group setting allows people to share their own experiences and gain confidence. Participants wished they had attended such a course when first diagnosed, which could have improved their self-management. However, some participants who were approached for interviews reported language or memory problems, which limited the impact of a stand-alone group course and its ability to help them manage behaviour changes in practice.

At the final follow-up, there were no significant differences between the SMILE (UK) group and the TAU group in QOLIE-31-P or any secondary outcome measures. The cost-effectiveness analysis showed that offering SMILE (UK) to epilepsy patients is cost-saving, but does not result in more QALYs than TAU.

A limitation of the SMILE (UK) evaluation is using self-reported data to measure outcomes. This can be problematic in a patient group who report memory problems when follow-up is > 12 months. However, for some outcomes, such as seizure frequency, there is no reliable alternative. The courses were held on weekdays, which may have limited the attendance of people who have work and family commitments. Our group had epilepsy for a median of 18 years and a 2-day course may be too little too late to change behaviour. In addition, about half of the group displayed some symptoms of anxiety and around 30%
had depression symptoms. Disturbed mood can also be associated with self-reported memory impairment. A psychological component in addition to a self-management course may be necessary for behaviour change.

A strength of the trial was the study design with its large sample size, generalisable to other populations. In addition, the study included a cost-effectiveness and process evaluation, and an assessment of implementation fidelity of a self-management course in epilepsy, which, to our knowledge, are the first of their kind.

**Recommendations for research**

A group course can help PWE overcome a sense of isolation and loss of self-esteem, probably when newly diagnosed. This research shows that psychological distress is strongly associated with impaired QoL. Based on this, psychological interventions could be tested for PWE with psychological comorbidity. A combination of educational, psychological and peer-group work interventions could be tested also within an integrated primary–secondary care context. This study highlighted the need for research on appropriate outcome measures in this population.

**Trial registration**

This trial is registered as ISRCTN57937389.

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