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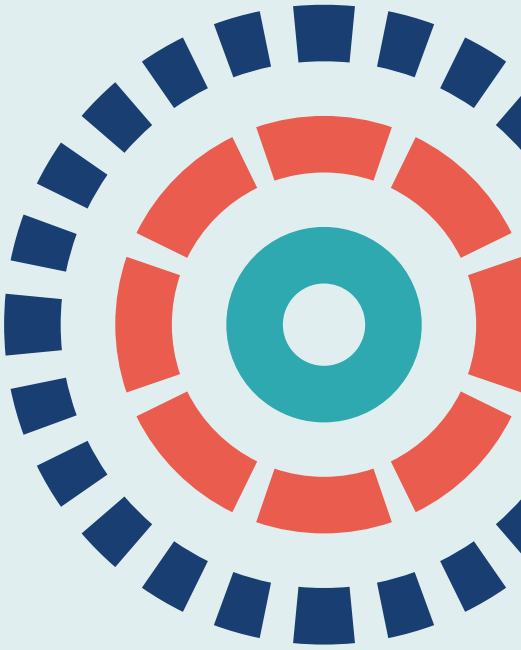

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Seizure first aid training for people with epilepsy attending emergency departments and their significant others: the SAFE intervention and feasibility RCT

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This report

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Abstract

Seizure first aid training for people with epilepsy attending emergency departments and their significant others: the SAFE intervention and feasibility RCT

Adam Noble[1*] Sarah Nevitt[2] Emily Holmes[3] Leone Ridsdale[4] Myfanwy Morgan[5] Catrin Tudur-Smith[2] Dyfrig Hughes[3] Steve Goodacre[6] Tony Marson[7] and Darlene Snape[1]

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Background: No seizure first aid training intervention exists for people with epilepsy who regularly attend emergency departments and their significant others, despite such an intervention's potential to reduce clinically unnecessary and costly visits.

Objectives: The objectives were to (1) develop Seizure first Aid training For Epilepsy (SAFE) by adapting a broader intervention and (2) determine the feasibility and optimal design of a definitive randomised controlled trial to test SAFE's efficacy.

Design: The study involved (1) the development of an intervention informed by a co-design approach with qualitative feedback and (2) a pilot randomised controlled trial with follow-ups at 3, 6 and 12 months and assessments of treatment fidelity and the cost of SAFE's delivery.

Setting: The setting was (1) third-sector patient support groups and professional health-care organisations and (2) three NHS emergency departments in England.

Participants: Participants were (1) people with epilepsy who had visited emergency departments in the prior 2 years, their significant others and emergency department, paramedic, general practice, commissioning, neurology and nursing representatives and (2) people with epilepsy aged $\geq$ 16 years who had been diagnosed for $\geq$ 1 year and who had made two or more emergency department visits in the prior 12 months, and one of their significant others. Emergency departments identified ostensibly eligible people with epilepsy from attendance records and patients confirmed their eligibility.

Interventions: Participants in the pilot randomised controlled trial were randomly allocated 1 : 1 to SAFE plus treatment as usual or to treatment as usual only.

Main outcome measures: Consent rate and availability of routine data on emergency department use at 12 months were the main outcome measures. Other measures of interest included eligibility rate, ease with which people with epilepsy could be identified and routine data secured, availability of self-reported emergency department data, self-reported emergency department data's comparability with routine data,

SAFE's effect on emergency department use, and emergency department use in the treatment as usual arm, which could be used in sample size calculations.

Results: (1) Nine health-care professionals and 23 service users provided feedback that generated an intervention considered to be NHS feasible and well positioned to achieve its purpose. (2) The consent rate was 12.5%, with 53 people with epilepsy and 38 significant others recruited. The eligibility rate was 10.6%. Identifying people with epilepsy from attendance records was resource intensive for emergency department staff. Those recruited felt more stigmatised because of epilepsy than the wider epilepsy population. Routine data on emergency department use at 12 months were secured for 94.1% of people with epilepsy, but the application process took 8.5 months. Self-reported emergency department data were available for 66.7% of people with epilepsy, and people with epilepsy self-reported more emergency department visits than were captured in routine data. Most participants (76.9%) randomised to SAFE received the intervention. The intervention was delivered with high fidelity. No related serious adverse events occurred. Emergency department use at 12 months was lower in the SAFE plus treatment as usual arm than in the treatment as usual only arm, but not significantly so. Calculations indicated that a definitive trial would need ≈ 674 people with epilepsy and ≈ 39 emergency department sites.

Limitations: Contrary to patient statements on recruitment, routine data secured at the pilot trial's end indicated that $\approx 40\%$ may not have satisfied the inclusion criterion of two or more emergency department visits.

Conclusions: An intervention was successfully developed, a pilot randomised controlled trial conducted and outcome data secured for most participants. The consent rate did not satisfy a predetermined 'stop/go' level of $\geq 20\%$. The time that emergency department staff needed to identify eligible people with epilepsy is unlikely to be replicable. A definitive trial is currently not feasible.

Future work: Research to more easily identify and recruit people from the target population is required.

Trial registration: Current Controlled Trials ISRCTN13871327.

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Contents

List of tables xi

List of figures xiii

List of supplementary material xv

List of abbreviations xvii

Plain English summary xix

Scientific summary xxi

Chapter 1 Introduction 1
Primary objectives 1
Secondary objectives 1
Background 1
Epilepsy and its epidemiology 1
Use of emergency hospital services for epilepsy and societal implications 2
Emergency department use for epilepsy is often clinically unnecessary but attendees often require more support 2
Epilepsy as one area where opportunities exist to reduce demands 3
The importance of seizure management skills and confidence in emergency health-care service use 4
Epilepsy self-management and support currently offered to people with epilepsy and their significant others 5
What is the evidence that self-management skills, including seizure management, can be modified? 6
Development of the SAFE intervention 7
Background to the existing seizure management course and its development 7
The need for a pilot randomised controlled trial of the SAFE intervention 9

Chapter 2 Part A: intervention development 11
Introduction 11
Methods 11
Participant settings and samples 12
Developing the intervention 14
Analytic process 15
Results 15
Health-care professionals 15
Changes made by intervention development panel to create version 1.1 17
Service users 22
Changes made by the intervention development panel to create version 1.2 24
Discussion 24

Chapter 3 Part B: pilot RCT – methods **25**
Introduction 25
Design 25
Study setting and population 25
Centres 25
Participant inclusion criteria 27
Participant exclusion criteria 27
Screening 27
Randomisation 28
Blinding and protection from bias 29
Intervention delivery 29
Data collection tools and follow-up visits 30
Primary 30
Secondary 30
Adverse events 33
Defining the outcomes 34
Primary 34
Secondary 34
Adverse events 34
Sample size 34
Completion of follow-ups 34
Data management 35
Data analysis 35
Rates of eligibility, consent, recruitment, retention and unblinding 35
Demographic and baseline characteristics 36
Primary outcome: epilepsy-related emergency department visits 36
Secondary outcome measures 37

Chapter 4 Part B: pilot RCT – recruitment, retention, intervention delivery and participant baseline characteristics **39**
Introduction 39
Participant flow through study 39
Recruitment rates and speed of recruitment 39
Randomisation 42
Receipt of intervention 42
Withdrawals and completion of follow-ups 42
Securing outcome data and their completeness 44
Baseline characteristics 44
Emergency department use in 12 months prior to enrolment 51
Researcher unblinding 53
Summary 53

Chapter 5 Intervention fidelity **57**
Introduction 57
Methods 57
Developing the intervention fidelity measurement instruments 57
Adherence 57
Competence 58
Testing the measures 58
Data analysis 58
Testing the measures 58
Course fidelity 58

Results 58
Testing the fidelity instruments 58
Course fidelity 59
Summary 59

Chapter 6 Outcomes of the pilot randomised controlled trial and implications for a definitive trial **61**
Introduction 61
Outcome measures 61
Safety and adverse events 64
Participant feedback 64
Sample size calculation for future trial 67
Summary 67

Chapter 7 Economic evaluation **69**
Introduction 69
Methods 69
Step 1: identification of resources 69
Step 2: measurement 70
Step 3: valuation 70
Analysis 70
Results 72
Discussion 75

Chapter 8 Discussion **77**
Principal findings 77
Part A: intervention development 77
Part B: pilot randomised controlled trial 77
Positives for feasibility of a definitive trial 77
Negatives for feasibility of a definitive trial 79
Possible modifications to address negatives for progression to definitive trial 80
Alternative steps to the diffusion of the SAFE intervention 82
Strengths and limitations 83
Intervention development 83
Pilot trial 84
Implications for NHS service commissioning, policy and practice 85
Recommendations for research 85

Acknowledgements **87**

References **91**

Appendix 1 Possible ways that the SAFE course could reduce unnecessary/avoidable emergency department use **107**

Appendix 2 Participant information sheet for health-care professional representatives (part A) **109**

Appendix 3 Participant information sheet for service user representatives (part A) **113**

Appendix 4 Topic guide for interviews with health-care professional representatives (part A) **119**

Appendix 5 Topic guide for focus groups with service user representatives (part A) **123**

Appendix 6 Search criteria employed at the different recruitment sites to identify potentially suitable persons attending emergency departments for epilepsy **127**

Appendix 7 Participant information sheet for patients in the pilot randomised controlled trial (project part B) **129**

Appendix 8 Full details of secondary outcome measures **135**

Appendix 9 Serious adverse event protocol **137**

Appendix 10 Cumulative, actual and expected recruitment (consented and randomised) to SAFE trial **141**

Appendix 11 Reasons for withdrawal from the pilot randomised controlled trial **143**

Appendix 12 Milestones in securing data from NHS Digital **145**

Appendix 13 Completeness of secondary outcome measures by assessment point, tool and participant type **149**

Appendix 14 Bland–Altman plot of agreement between self-reported and Hospital Episode Statistics data on emergency department visits at baseline, without any exclusions **153**

Appendix 15 Demographic characteristics of significant other participants **155**

Appendix 16 Adherence ratings for each checklist item and module **157**

Appendix 17 Number of self-reported epilepsy-related emergency department visits **159**

Appendix 18 Baseline scores of patient participants and significant other participants and change over follow-up period on secondary outcome measures **161**

Appendix 19 Adverse events occurring during pilot trial in descending order, according to frequency overall **189**

List of tables

TABLE 1 Epilepsy training materials 8

TABLE 2 Health-care professional consultation: groups supporting PWE 12

TABLE 3 Content of original course and revisions made following feedback 18

TABLE 4 Self-reported outcome measures by assessment and participant type 31

TABLE 5 Attendance at ED not related to epilepsy 40

TABLE 6 Other reasons for non-eligibility (individuals visiting for established epilepsy) 41

TABLE 7 Reasons for non-eligibility (ostensibly eligible individuals) 41

TABLE 8 Reasons for declining participation (eligible individuals) 41

TABLE 9 Number of patient participants fully completing study assessment tools at each time point 45

TABLE 10 Number of SO participants fully completing study assessment tools at each time point 46

TABLE 11 Demographic characteristics of patient participants 46

TABLE 12 Baseline disease characteristics and key health service use of patient participants 48

TABLE 13 Demographic characteristics of eligible participants by agreement to participate in the trial 54

TABLE 14 Characteristics of the courses 59

TABLE 15 Number of ED visits patient participants made according to HES data 61

TABLE 16 Differences between groups in number of HES-recorded ED visits: SAFE plus TAU vs. TAU alone 62

TABLE 17 Differences between groups in number of self-reported ED visits: SAFE plus TAU vs. TAU alone 63

TABLE 18 Comparison of HES-recorded and self-reported ED visits during the 12 months post randomisation 64

TABLE 19 Feedback on participation in the SAFE trial: patient participants 66

TABLE 20 Feedback on participation in the SAFE trial: SO participants 66

TABLE 21 Required sample size for a definitive trial to detect estimated effect of SAFE plus TAU on ED use (measured using HES data) **67**

TABLE 22 Unit costs **71**

TABLE 23 Total observed costs and cost per delegate to deliver SAFE **73**

List of figures

FIGURE 1 Intervention development process 11

FIGURE 2 Schematic of planned design for part B of the project: trial approval and monitoring 26

FIGURE 3 The CONSORT flow diagram of eligibility screening for the trial 40

FIGURE 4 The CONSORT flow diagram for the SAFE trial 43

FIGURE 5 Histogram of the number of ED attendances in the previous 12 months by patients according to HES system 51

FIGURE 6 Bland–Altman plot of agreement between self-reported and HES data on ED visits at baseline ($n = 41$; excludes outlier) 52

FIGURE 7 Bland–Altman plot of agreement between self-reported and HES-recorded ED visits at 12 months ($n = 34$) 65

FIGURE 8 Workflow 69

List of supplementary material

Report Supplementary Material 1 The SAFE study trainer manual

Report Supplementary Material 2 The SAFE study TIDieR checklist

Report Supplementary Material 3 The SAFE study CONSORT checklist

Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/hsdr08390).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

List of abbreviations

A&E	accident and emergency department
APEASE	Affordability, Practicality, Effectiveness and cost-effectiveness, Acceptability, Side-effects/safety and Equity
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
CR	central range
CRF	clinical research form
CTU	Clinical Trials Unit
ED	emergency department
ES	Epilepsy Society
FG	focus group
GP	general practitioner
GCSE	General Certificate of Secondary Education
HADS	Hospital Anxiety and Depression Scale
HES	Hospital Episode Statistics
IMD	Index of Multiple Deprivation
IQR	interquartile range
NASH	National Audit of Seizure management in Hospitals
NBR	negative binomial regression
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NVQ	National Vocational Qualification
O level	Ordinary level
PABAK-OS	prevalence-adjusted bias-adjusted kappa for ordinal scales
PWE	people with epilepsy
QOLIE-31-P	Quality of Life in Epilepsy Scale-31 item-Patient-weighted
RCT	randomised controlled trial
REC	research ethics committee
SAE	serious adverse event
SAFE	Seizure first Aid training For Epilepsy
SD	standard deviation
SMILE	Self-Management education for adults with poorly controlled epILEpsy
SO	significant other
TAU	treatment as usual
TIDieR	Template for Intervention Description and Replication
VAT	value-added tax

Plain English summary

Limited knowledge of how to manage seizures leads some individuals with epilepsy to visit emergency departments following seizures despite not needing medical attention. Such visits are expensive for the NHS and can be inconvenient for patients.

Part A of this project aimed to develop a self-management course for patients frequently visiting emergency departments for epilepsy, as well as for their significant others, such as family and friends. Having developed the course, a large trial was needed to find out if it would be beneficial. Before doing that we needed to answer the following question: 'can such a trial be done?'. Part B of this project aimed to answer this by conducting a 'pilot randomised controlled trial'. A pilot is like a practice run.

In part A, nine health-care professionals and 23 service users helped us to develop the course, which we called Seizure first Aid training For Epilepsy (SAFE). They considered it acceptable and NHS feasible.

In part B, 53 patients diagnosed with epilepsy (and 38 significant others) were recruited from three emergency departments. Patients were randomly assigned to either an invitation to attend SAFE (with or without their significant other) or usual treatment only. All participants took their medication as usual. Participants were asked to complete questionnaires on their use of emergency departments and confidence managing seizures 3, 6 and 12 months later.

The pilot trial found that emergency departments could not easily identify people to invite, and fewer people agreed to take part than expected (12.5% rather than at least 20%). Those who did take part tended to participate for the full length of the trial, and information on their use of emergency departments 12 months later was obtained in over 90% of cases. Nearly all participants said that they would take part in such a trial again.

Even though parts A and B were carried out successfully, it was difficult to identify potential participants and fewer people agreed to participate than we expected, so a large trial, as currently designed, is not feasible.

Scientific summary

Background

Epilepsy is one of the UK's most common serious brain disorders. Up to 20% of people with epilepsy visit hospital emergency departments each year, approximately 60% of whom do so multiple times. These visits are expensive for the NHS; half result in hospital admission.

People with epilepsy visiting emergency departments report more seizures, anxiety and stigma and are more likely to live in a socially deprived area than those in the wider epilepsy population. Identifying people with epilepsy who visit emergency departments can be challenging; most are unknown to specialist epilepsy services and are not referred on to them following emergency department visits. General practitioners are also not always informed of the contact that people with epilepsy have with emergency services.

National Audit of Seizure Management in Hospitals data and similar data indicate that many emergency department visits by people with epilepsy are clinically unnecessary. This is because most of these emergency department attendees have known, rather than new, epilepsy and have experienced uncomplicated seizures. Although frightening, such seizures can be managed by people with epilepsy and their family and friends without medical attention, as guidelines state.

Emerging evidence suggests that people with epilepsy and their significant others, to whom care decisions can be delegated, have low confidence in their own seizure management, which may explain why some people with epilepsy make clinically unnecessary visits. Offering people with epilepsy who frequently attend emergency departments, and their significant others, a self-management intervention that improves their confidence and ability to manage seizures may lead to fewer visits.

We report a project seeking to develop the first such intervention: Seizure first Aid training For Epilepsy (SAFE). To develop the intervention, an existing group-based seizure management course, which is offered by the Epilepsy Society (www.epilepsysociety.org.uk; Chalfont St Peter, UK) in the voluntary sector to a broader audience, was adapted. A pilot randomised controlled trial of SAFE was then conducted. A pilot was appropriate because the feasibility and optimal design of a definitive trial was unclear.

Aim and objectives

Part A: intervention development

- Optimise the content, delivery and behaviour change potential of the Epilepsy Society's course for people with epilepsy attending an emergency department and their significant others.

Part B: pilot randomised controlled trial

- Conduct an external pilot randomised controlled trial of SAFE plus treatment as usual versus treatment as usual only to estimate recruitment, consent and follow-up rates in a definitive trial.
- Estimate the annual rate of emergency department visits in the treatment as usual arm and the dispersion parameter to inform the sample size calculation of a definitive randomised controlled trial.

- Test the acceptability of the randomisation to participants.
- Evaluate SAFE's implementation fidelity in the pilot randomised controlled trial.
- Analyse the cost of implementing the SAFE programme.

Methods and analysis

Part A: intervention development

Design

An experience-based co-design approach comprising three iterative stages identified the changes required to the Epilepsy Society's intervention: stage 1 – leading representatives from professional groups supporting people with epilepsy reviewed the course materials and were interviewed about the changes needed; stage 2 – the Epilepsy Society's original intervention was not underpinned by a clear behaviour change mode and, therefore, the intervention's behaviour change potential was optimised; stage 3 – focus group discussions took place with service user representatives who received an initial adaption of the intervention. Data from the different stages were captured using audio-recordings, thematically analysed and considered by a multidisciplinary intervention panel.

Recruitment

A purposive sample of representatives from neurology, emergency medicine, the ambulance service, specialist nursing, general practice, user groups and health-care commissioning was recruited with the help of professional organisations. Epilepsy user groups helped to recruit service user representatives. To be eligible, user representatives (be they a person with epilepsy or one of their significant others) needed to be aged $\geq$ 16 years and able to provide informed consent. User representatives who were people with epilepsy needed to have visited an emergency department in the previous 2 years for epilepsy.

Part B: pilot randomised controlled trial

Design

The design was an external pilot randomised controlled trial. Recruited people with epilepsy (and their significant other if they took part with one) were randomised to receive SAFE plus treatment as usual or treatment as usual only. The SAFE programme was delivered by an epilepsy nurse in a hospital's educational centre. Participants allocated to treatment as usual received SAFE only after the trial finished.

The proposed primary outcome measure for a definitive trial of SAFE is emergency department use in the 12 months following randomisation measured using routine hospital data. In the pilot trial this was captured by Hospital Episode Statistics. Participants provided consent for the release of these data. Proposed secondary outcomes included self-reported emergency department use, fear of seizures, knowledge and confidence managing seizures, quality of life, distress, seizures, stigma, carer burden, service use and adverse events. These were measured by a researcher, blind to treatment allocation, who completed questionnaires with participants at 3, 6 and 12 months post randomisation. At the assessment at 12 months, participants also provided feedback on trial participation.

Rates of recruitment and retention were calculated, as was the emergency department event rate in the control arm. Emergency department visits measured using routine hospital data for the 12 months prior to and 12 months following randomisation were also compared with self-reported emergency department visits for these periods. The estimates from the pilot trial were evaluated against two predetermined 'stop/go' progression criteria for a full trial: $\geq$ 20% of eligible people with epilepsy needed to agree to take part and primary outcome data at 12 months needed to be secured for $\geq$ 75% of people with epilepsy. Although the trial was not designed to detect a clinically important difference in emergency department use, an estimate of SAFE's effect on this measure was also calculated to help to inform the possible design of a future trial.

It was anticipated that 12 months of attendances at three NHS type 1 emergency departments would be sufficient to secure a sample of 80 people with epilepsy for the pilot trial, with 40 people with epilepsy in each treatment arm, permitting the study to estimate a drop-out rate of 25% (with a 95% confidence interval of 10%) and a consent rate of 20% (with a 95% confidence interval of 4%). Assuming data on emergency department use at 12 months were not available for 25% of people with epilepsy, outcome data from 60 people with epilepsy would still allow for robust estimation of the emergency department rate and dispersion parameter.

Measures of implementation fidelity (adherence and competence) for SAFE were developed and their inter-rater reliability assessed. Adherence was assessed by a checklist of the items constituting the intervention. Competence was measured by calculating facilitator speech during the intervention (didacticism). The measures were then used by independent raters, who listened to audio-recordings of all trial SAFE sessions.

A microcosting exercise calculated the fixed and variable costs of delivering SAFE. The process involved a health economics researcher meeting with intervention staff and mapping out the work and resources required for each of the courses run. The cost of developing SAFE was also determined.

Recruitment

Using electronic attendance records and triage cards, local principal investigators at three NHS type 1 emergency departments in north-west England retrospectively identified people with epilepsy who had visited emergency departments in the previous 12 months for epilepsy and posted an invitation letter. Inclusion criteria were an age of $\geq$ 16 years, an established diagnosis of epilepsy ($\geq$ 1 year), an antiepileptic medication prescription, reported visits to an emergency department on two or more occasions in the previous 12 months, and the ability to provide informed consent, participate in SAFE and complete questionnaires in English. Those receiving an invitation letter were instructed that if they were not interested in taking part in the trial or not eligible that they should opt out of further contact within 3 weeks. A research worker telephoned those not opting out to explain the study further and verify patient eligibility and willingness to participate. The research worker met with those who wanted to take part and their significant others, and secured informed consent and completed baseline questionnaire assessments.

Results

Part A: intervention development

Over a period of 8 months, feedback from nine representatives from different professional groups, 13 people with epilepsy and 10 significant others was secured and the finalised SAFE intervention developed.

During stage 1, health-care professionals considered the Epilepsy Society's course to provide a good foundation but requested changes to its language and presentation style to make it less didactic and to emphasise the benefits to service users. They recommended the inclusion of new content to elicit and address service users' fears relating to seizures. To promote consistency and make the intervention suitable for delivery in the NHS, a trainer's manual was also developed. During stage 2, the behaviour change potential of the intervention was optimised. Specifically, the intervention development panel considered self-affirmation theory to be pertinent because the course would highlight to some participants that their past behaviour conflicted with medical guidance. To mitigate against the defensive processing of information that, according to the theory, can result, a brief kindness questionnaire was inserted at the intervention's start. During stage 3, service users reported having a positive view of the intervention, its videos and the associated educational materials. Their feedback resulted in changes to the order of the content, the addition of information relating to post-ictal states and the generation of a website that held the content of the course to mitigate the effect of memory difficulties and to allow the information to be shared with other significant others.

The finalised SAFE intervention was intended for delivery to groups of up to 10 patient–carer dyads by a single facilitator with knowledge of epilepsy and to last ≈ 4 hours, including breaks. It contained six modules centred around basic epilepsy and first aid knowledge, the recovery position, informing others about epilepsy and how to help if seizures occur, medical identifications, seizure triggers and home safety. Materials included presentation slides and professionally produced videos. The total cost of developing SAFE was £9947.

Part B: pilot randomised controlled trial

Fifty-three people with epilepsy and 38 of their significant others were recruited over ≈ 7.5 months. The consent rate (12.5%, 95% confidence interval 9.3% to 15.6%) and eligibility rate (10.6%, 95% confidence interval 9.6% to 11.5%) were low. Despite an amendment to extend the period within which people with epilepsy could be identified from emergency departments (i.e. the previous 18 months rather than the previous 12 months of attendances), the intended sample size could not be recruited.

A lack of granularity by which attendances were coded in the emergency departments' record systems meant that identifying people with epilepsy was resource intensive, requiring ≈ 3 days of a local principal investigator's time at each site. Contacting patients by telephone was also challenging. The researcher made successful contact with only 47.8% of eligible patients.

The mean age of the people with epilepsy recruited was 39.9 years, 29 (56.9%) were female and most lived in areas of high levels of social deprivation. The median time since diagnosis was 21 years. Those recruited were similar in age and social deprivation to those declining participation. The recruited sample might not have been representative of the target population in sex. Moreover, 74.5% reported seeing an epilepsy specialist in the previous 12 months, which is higher than expected.

Of those recruited, 51 people with epilepsy (and 37 significant others) were randomised: 26 people with epilepsy (and 18 significant others) to SAFE plus treatment as usual and 25 people with epilepsy (and 19 significant others) to treatment as usual only. The demographics, disease characteristics and scores on the assessment tools at baseline were similar in each treatment arm, but there was some imbalance in prior emergency department use. Most people with epilepsy (76.9%) randomised to SAFE received the intervention and it was found to have been delivered with high fidelity. No participants allocated to treatment as usual attended a SAFE course by mistake. Delivering SAFE was estimated to cost £333 per patient (with or without a significant other) and it is plausible that it could be delivered for as little as £261 per patient.

Routine data on emergency department use at 12 months were secured for 94.1% of people with epilepsy, but obtaining it took 8.5 months and was resource intensive, and the application for these data was initially rejected by NHS Digital on the basis of what proved to be incorrect reasoning. Self-reported emergency department data at 12 months were secured for only 66.7% of people with epilepsy. It was found that participants reported more emergency department visits than were recorded in routine data. For the 12 months prior to randomisation, participants reported 3.8 more emergency department visits on average than were recorded in routine data.

Negative binomial regression estimated emergency department use at 12 months to be, according to routine data, ≈ 47% lower in the SAFE plus treatment as usual arm than in the treatment as usual only arm, but not significantly so. In the SAFE plus treatment as usual arm, emergency department use reduced from 2.1 visits over a 12-month period to 1.8 visits; in contrast, the mean number of visits in the treatment as usual arm increased from 3 to 3.4.

No serious adverse events related to participation occurred, and all but one of the 32 (68.1%) people with epilepsy and the 20 (62.5%) significant others providing feedback on trial participation said that they would participate again, with SAFE participants valuing the intervention.

The estimated effect of SAFE on emergency department use and the dispersion parameter in the control arm ($k = 0.69$, range 0.17 to 1.21) indicated that a definitive trial of SAFE's efficacy would require a sample of ≈ 674 people with epilepsy. The consent rate in the pilot indicates that it would need ≈ 39 emergency department recruitment sites.

Conclusions

The co-design approach allowed for a brief, manualised intervention that was supported by stakeholders and based on an NHS-feasible delivery method to be rapidly developed.

A pilot randomised controlled trial was conducted successfully. Persons from the target population could be identified, recruited, randomised and treated as intended. Outcome data for the proposed primary outcome measure could be secured for most participants and meant that the trial satisfied the predetermined 'stop/go' criterion of $\geq 75\%$.

However, the consent rate for the pilot trial was low and meant that the second 'stop/go' criterion of $\geq 20\%$ was not met. The low consent rate raises concerns about the representativeness of the sample that would be recruited into a definitive trial and its external validity. The low consent rate also means that a definitive trial would require a larger number of recruitment sites than most definitive trials and be expensive. It may even not be possible to secure the required emergency departments to act as recruitment sites because the resources required from them to identify participants may be prohibitive.

Implications for NHS service commissioning, policy and practice

- The trial was not designed to determine SAFE's efficacy. There remains limited evidence to justify the commissioning of such a service.
- Some people with epilepsy are unknown to ambulatory care services and cannot be readily identified. Increasing the granularity with which attendances at emergency departments are coded could enable them to be readily identified, supported and involved in research.
- Using routine data on emergency department use in trials could make trials less vulnerable to losses to follow-up and mean that trials are not exposed to apparent recall bias. However, stakeholders need to be given more assurances from those holding the data that the data are likely to be provided, and provided in a timely manner.
- A case can be made for converting SAFE into a free online resource to which people could be directed in the short term, going some way to address the otherwise unmet seizure first aid training needs of people with epilepsy who visit emergency department and their significant others.

Recommendations for further research

- A full definitive trial of SAFE, with the current design, is not feasible.
- Research to determine how people from the target population can be better recruited is required.
- Converting SAFE into a free online resource could provide an opportunity for an alternative method of evaluating its effect. Via a pre–post design, persons accessing the online resource could complete brief measures to assess change in seizure first aid confidence and skills and give their consent for researchers to access routine data on their use of emergency departments before and after viewing the resource.

Trial registration

This trial is registered as ISRCTN13871327.

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Chapter 1 Introduction

This project sought to develop and pilot seizure first aid training for adults with established epilepsy who frequently visit hospital emergency departments (EDs) and their significant others (SOs). It had two parts and used mixed methods. In part A, we developed the intervention: Seizure first Aid training For Epilepsy (SAFE). This was done by adapting a broader course that was being offered by the Epilepsy Society (ES) (www.epilepsysociety.org.uk; Chalfont St Peter, UK). Part B was a pilot randomised controlled trial (RCT) of the SAFE intervention with people with epilepsy (PWE) from the target population and their SOs, with the aim of assessing the feasibility and optimum design of a definitive RCT to test SAFE's efficacy.

The primary and secondary objectives for the project are described here.

Primary objectives

Part A: intervention development –

- optimise content, delivery and behaviour change potential of the ES's course for PWE attending an ED, and their SOs.

Part B: pilot RCT –

- conduct a pilot RCT of SAFE plus treatment as usual (TAU) versus TAU only to estimate probable recruitment, consent and follow-up rates in a definitive trial.

Secondary objectives

Part B: pilot RCT –

- calculate estimates of the annual rate of ED visits in the TAU arm and dispersion parameter to inform the sample size calculation of a definitive RCT
- test the acceptability of randomisation to participants
- evaluate SAFE's implementation fidelity in the pilot RCT
- analyse the cost of implementing the SAFE programme.

In this chapter, the rationale for providing seizure first aid training is provided, we describe how the existing intervention was adapted and we outline why a pilot RCT, rather than proceeding straight to a definitive trial, was appropriate.

Background

Epilepsy and its epidemiology

With a prevalence of ≥ 1% in the UK,[1–3] epilepsy is the UK's second most common serious neurological condition.[4]

The International League Against Epilepsy (Flower Mound, TX, USA) defines a person as having epilepsy if they experience two or more unprovoked (or reflex) seizures more than 24 hours apart or if they have experienced one such seizure and the probability of them experiencing another over the next 10 years is akin to that of a person who has experienced two (i.e. ≥ 60%).[5]

Epilepsy's aetiology is variable. It can, for example, arise as a consequence of cerebrovascular disease, head trauma, congenital abnormalities and neurodegenerative disease, or be idiopathic.[6] Mortality risk varies for PWE but, with a standardised mortality ratio of ≈ 2.2, it is higher than that in the general population.[7,8]

Trial data indicate that most PWE (≈ 70%) can theoretically become 'seizure free' via treatment, typically using antiepileptic drugs. However, up to 48% of PWE in the UK continue to experience seizures.[9] However, epilepsy is more than 'just' seizures. This is reflected in the International League Against Epilepsy's definition of epilepsy as 'a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological, and social consequences of this condition'.[10] The diagnosis itself can be associated with significant psychological and social costs for the individual. Being labelled negatively as 'epileptic' can be accompanied by discrimination,[11,12] with potential detrimental effects on education, unemployment and driving. Around 30% of PWE also meet diagnostic criteria for an anxiety and/or depressive disorder. All undermine well-being.[9,13,14]

Use of emergency hospital services for epilepsy and societal implications

Epilepsy has societal impacts. One of these is the cost of providing health care. In the European Union, the total cost of epilepsy in 2004 was €15.5B,[15] with a cost per case of €2000–11,500. One costly element is the provision of emergency care, which international evidence shows PWE frequently utilise.

In the UK, ≤ 20% of PWE visit a hospital ED for epilepsy each year.[16–18] Most (≈ 90%) are transported there by an emergency ambulance.[19–21] The 2015/16 cost of providing emergency care to PWE in England was estimated to be at least £70M (excluding indirect costs).[22]

Costs are high in part because half of ED attendances by PWE result in hospital admission.[16,19,23] Indeed, 85% of all admissions for epilepsy occur on such an unplanned basis.[24] Among chronic ambulatory care sensitive conditions, epilepsy is the second most common cause of unplanned admissions (17%).[25–27]

Reattendance also drives up costs. The exact distribution of ED use for epilepsy is unclear, but it is apparent that reattendance rates are high. The 2014 UK-wide National Audit of Seizure management in Hospitals (NASH)[28] examined data from ≈ 4000 seizure-related ED attendances from 85% of acute hospitals. Among those with established epilepsy, 60% had attended the same ED as a result of a seizure in the previous 12 months.[20] Whitson *et al.*[29] found epilepsy to be the most frequent neurological reason for emergency readmission into UK hospitals. Dickson *et al.*'s[30] findings are also instructive: they examined data on unplanned admissions in hospitals in England for suspected seizures of any cause (not just epilepsy) in adults between 2007 and 2013. They found that 22.4% of patients had more than one admission per year and that there was a 34% chance of readmission within 6 years.

The most detailed evidence on ED use among PWE comes from a previous National Institute for Health Research (NIHR)-funded study (reference identifier 08/1808/247) by Ridsdale *et al.*[27,31,32] This study prospectively recruited 85 PWE from three London EDs and asked them to self-report on ED use in the prior 12 months; 60% reported multiple ED attendances,[27] 25% reported two attendances and 36% reported at least three attendances. The median number of visits for those who had made multiple visits was two [interquartile range (IQR) 2–5]. This pattern contrasts with that seen in the general ED population. Moore *et al.*[33] reported that only 24% of people from the general ED population reattend London EDs within 12 months.

Emergency department use for epilepsy is often clinically unnecessary but attendees often require more support

Seeking emergency care for epilepsy can be important, even life-saving. Reasons include a first seizure and status epilepticus. Some ED visits by PWE are for these reasons; most are not. The NASH,[20,21,28] for example, found that most people attending an ED for a suspected seizure had diagnosed, rather than new,

epilepsy. Moreover, most appear to have experienced an uncomplicated seizure. Dickson *et al.*[34] reviewed records for 178 seizure incidents presenting to one regional ambulance service over 1 month in 2012. Medical emergencies were uncommon and seizures had self-terminated before the emergency vehicle arrived in > 90% of cases. In only 8% of incidents were emergency drugs required to terminate the seizure. Uncomplicated seizures in someone with established epilepsy, although potentially frightening and distressing to experience and observe, do not typically require the full facilities of an ED and can be managed within the community by the person with epilepsy and their SOs. Indeed, going to an ED in these circumstances may result in iatrogenic harms caused by unnecessary investigations and interventions (e.g. unused intravenous cannulations, unnecessary head computerised tomography scans).[35–37]

Although a high proportion of epilepsy-related ED visits do result in hospital admission, most appear unnecessary,[38] with factors beyond the patient's clinical need appearing to play a role in why the admission occurred (e.g. lack of access to senior medical review, need to avoid breaches of ED waiting-time targets).[39]

Although the acute episodes leading PWE to visit an ED do not typically require the facilities of an ED, PWE attending an ED do often have poorer health than those in the wider epilepsy population. They report more seizures, poorer quality of life, less epilepsy knowledge, more anxiety and feeling more stigmatised because of epilepsy.[27,40–45] Despite this, most (≈ 65%) have not seen an epilepsy specialist in the prior 12 months.[28]

There is also inequality in the use of EDs, with attendees being more likely to reside in areas where social deprivation is high and seizure control worse.[41,46,47] Indeed, ED admissions for seizures vary by more than fivefold between geographical regions in England[42,44] and are most frequent in more socially deprived areas.[47,48]

The National Institute for Health and Care Excellence (NICE)[49] recommends that when seizures are not controlled a patient should be referred to specialist services. However, going to an ED because of an epileptic seizure does not typically lead to an increase in support. The NASH[20,28] found that most (80%) PWE are not seen by a specialist during their attendance, usual care providers are often not informed of the attendance and most (60%) PWE are not referred to a specialist for follow-up. Among PWE attending an ED, those living in the most deprived areas are among those least likely to be referred to a specialist for follow-up.[50]

Epilepsy as one area where opportunities exist to reduce demands

The NHS has been operating in a context of rising demand, slow funding growth and increasing operating costs. In 2015–16, this culminated in an aggregate funding deficit of £1.85B.[51,52] The NHS Plan,[53] *Five Year Forward View*[54,55] and related publications challenge the NHS to make substantial savings while working with patients and SOs to improve care experience and outcomes and reduce health inequalities. Epilepsy has been identified as one condition for which opportunities exist to improve patient outcome and experience, reduce demands and generate savings.[56]

Although there is a drive to reduce ED visits for epilepsy and enhance patient outcomes, it has been challenging to identify how to achieve this,[25,57] not least because the reason(s) for ED visits for epilepsy in publicly funded health-care systems has been unclear. The association between seizure frequency and ED use is, for example, only modest in size, and seizure type has not proved a robust predictor.[17,27,31,40]

Emerging evidence highlights the potential importance of a person's self-management skills in their use of EDs, specifically the confidence and skills that they and those around them have to manage seizures, with this potentially moderating the relationship between an uncomplicated seizure and the help sought at the time.

The importance of seizure management skills and confidence in emergency health-care service use

'Self-management' is a broad term. It refers to an 'individual's ability to manage their symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition'.[58] In the context of epilepsy, self-management of adult epilepsy has been defined as 'activities that an individual can perform alone that are known to either control frequency of seizures or promote well-being of the person with seizures'.[59]

Much of the evidence regarding the potential importance of self-management skills in ED use comes from Ridsdale *et al.*'s aforementioned NIHR study.[27,31,32] This study followed up its sample of 85 PWE for 12 months. A subgroup was interviewed about the reasons for their visits. Analyses indicated that participants fell into two groups. In the first were participants who reported high levels of confidence in managing their epilepsy. Their views closely aligned with seizure first aid guidelines. Explanations offered by these participants for their visits included having experienced an unusually long seizure or having sustained a significant injury. These persons had typically visited an ED only once in the previous 12 months.

By way of contrast, participants in the second group reported not feeling confident in managing seizures. They expressed a need for immediate access to urgent care when they had a seizure and had typically made two or more ED visits in the previous year. They explained that they and their family (to whom care decisions were often delegated when the patient was unconscious or lacked capacity) were fearful of seizures, including the possibility of death and brain damage, and were unsure about how to manage seizures and could not tell others about how to help should they have a seizure.[31,32] This, they reported, could lead them to call for an ambulance when they were about to have, or had had, a seizure. Despite having been diagnosed with epilepsy for an average of ≈ 10 years, these participants reported that they had not received sufficient information about epilepsy. Telling quotations from those interviewed included the following:[31,32]

> *[With] cancer, you're awake. I know you can die, but you're awake. I'd prefer something like that [. . .] Having epilepsy, you're going into a fit. You don't know if you're going to wake up or die. That's why I call [UK emergency services telephone number]!*
>
> *Patient 23*

> *[I was] just worried because I don't know anything about epilepsy [. . .] I only know the bad things [. . .] I know you can die [. . .] I am so worried I decided just to ring an ambulance [. . .] Better safe than sorry.*
>
> *SO 60*

Quantitative results from the study reinforced what participants said at interview. There was, for example, evidence of less first aid knowledge in the ED sample than in the wider epilepsy population. One-third of the ED sample incorrectly stated that it was always necessary to call a doctor or ambulance if a person with epilepsy has a seizure, even if it occurs without complications.[27] Only 11% of the wider epilepsy population believe this.[60]

Also important were the results of regression analyses to determine which baseline data could predict the number of ED visits participants reported 12 months later. A range of variables were examined for their association, including seizure frequency, seizure severity and medication management skills. It was participants' level of confidence about managing epilepsy (as measured by the Wagner 6-item Mastery Scale)[61] and the extent to which they felt stigmatised because of epilepsy (as measured by Jacoby's Stigma Scale of Epilepsy)[62] that were found to best predict ED use. These factors held similarly sized associations with ED use, with lower confidence (incidence rate ratio 0.86) and increased feelings of stigma (incidence rate ratio 1.32) being associated with more ED use.

'Mastery' refers to a state of confidence in which a person feels able to independently overcome the challenges with which they are faced.[63] The mastery measure captured the degree to which participants perceived themselves to have an internal or external locus of control, with example items from the scale including 'I often feel helpless in dealing with my seizures' and 'Sometimes I feel that my epilepsy controls my life'.[61] Evidence suggests that when a person feels more confident in their ability to cope and manage their illness effectively they are more likely to put self-management behaviours into practice.[64]

Epilepsy self-management and support currently offered to people with epilepsy and their significant others

The findings from Ridsdale *et al.*'s study[27,31,32] are in keeping with prior evidence: coping with life in the context of epilepsy requires an individual to accept their diagnosis and learn and adopt specific self-management behaviours to prevent seizures and manage consequences. These tasks together constitute what Corbin and Strauss[65] labelled the 'work' of living with a chronic condition.

It is for these reasons that NICE[49] recommends self-management support for PWE. Epilepsy specialist nurses form an important part of the way in which this support is delivered. However, it is known that current care models in the UK and beyond continue to fail some PWE and mean that these PWE have less than optimal levels of self-management confidence. In contrast to some other chronic conditions, there exists no routine course that PWE can go on to learn about their condition once diagnosed, and there is limited time in routine care appointments for advice on self-management.[66–68] Patients have previously summarised the lack of information and support that they were given following diagnosis as 'I was left high and dry'.[69,70] It is PWE with lower levels of formal education who have been found to have the least epilepsy knowledge.[71,72]

The role that Ridsdale *et al.*'s study[27,31,32] found a patient's family and friends to play when a seizure occurs also accords with wider evidence: despite greater social isolation, up to 90% of PWE can still identify a SO who acts as an informal carer.[73] These SOs are not always trained in the management of seizures, including in the use of emergency medications.

One reason that SOs have been largely missing from discussions about the causes for ED visits for epilepsy is that it has widely been thought that such visits primarily occur because the person with epilepsy was alone in a public place, had a seizure and an ambulance was called by a bystander, and because a lack of information about the person's medical history (such as from an epilepsy identification card) meant that paramedics transported the person to ED as a precaution.[74,75] Consequently, the focus has often been on how the public, rather than SOs, can be supported and educated.[76] Although ED visits for epilepsy certainly do occur via this route,[77,78] this seems to be the minority.

Reuber *et al.*[23] examined attendances at a large ED in Leeds, UK. They found that, in this area of the UK, only 15% of ED visits by PWE occurred because the person was alone and had a seizure in a public place. Most seizures leading to an ED visit instead occurred in the patient's home[23] and most (70%) 999 calls for seizures are made by relatives or friends rather than by members of the public.[34]

Given the indications that seizure management skills and confidence have an important role in emergency service use, a promising idea that has emerged is to offer PWE who frequently attend ED and their SOs a self-management intervention to improve their confidence and competence in managing seizures.[45,79] The objectives of self-management interventions are to facilitate patients taking an active role in their own health care by encouraging autonomy and providing accurate information on symptom management.[80] They are different from traditional educational approaches because, as well as educating, they seek to empower those living with chronic health-care conditions.[81] It is asserted that when people are supported to become more activated they benefit from better health outcomes and improved health-care experiences and make fewer unplanned health-care admissions.[80]

What is the evidence that self-management skills, including seizure management, can be modified?

Evidence from adult and paediatric literature at the time of project design

Evidence from the literature on self-management interventions for people living with other chronic conditions such as diabetes,[82,83] arthritis[84–86] and asthma[87–89] indicates that it is possible to elicit improvements in self-management. Consequently, in these fields self-management support has become well established.[90–96] In the UK, self-management courses have become freely accessible to people with diabetes.[97,98] The evidence base on improving self-management skills in PWE is more limited.

A Cochrane review by Bradley *et al.*[99] examined care delivery and self-management strategies for adults with epilepsy. It found four self-management studies focusing on adults with epilepsy.[100–103] None of the trialled programmes focused exclusively on seizure management or those attending EDs or systematically involved SOs, and none had been trialled in the UK. However, the review did conclude that there was tentative evidence that such interventions can improve epilepsy self-care skills.

Helgeson *et al.*'s[100] small US RCT is noteworthy because it evaluated an intervention that included some discussion of seizure first aid. The intervention, the Sepulveda Epilepsy Education programme, is a psychosocial 2-day group course.[100] At follow-up at 4 months, participants receiving the intervention demonstrated a statistically significant increase in their understanding of epilepsy, a decrease in seizure fear and a decrease in hazardous medical self-management practices compared with wait-list controls. However, health service utilisation was not measured and no significant changes were found in relation to anxiety or confidence managing epilepsy.

As the number of trials conducted with adults with epilepsy is small, Lindsay and Bradley's[104] Cochrane review of self-management interventions for children with epilepsy and their parents is instructive. Lindsay and Bradley identified two RCTs of interventions that contained modules on seizure first aid.

The first, conducted by Tieffenberg *et al.*,[87] evaluated a Spanish group-based programme, the Civil Association for Research and Development in Health (ACINDES in Spanish), for children aged 6–15 years and delivered by teachers to educate children and parents about epilepsy. It consists of five weekly 2-hour sessions, followed by a reinforcement session 2–6 months later. At follow-up at 12 months, children in the intervention arm showed statistically significant improvements in epilepsy knowledge compared with children in the control arm. There was also a significant reduction in ED visits. The mean number of ED visits made by children in the intervention arm in the 12 months prior to randomisation was 0.90. This reduced to 0.22 at follow-up at 12 months. For the TAU arm the mean number of ED visits made by children went from 0.83 to 0.46.

The second RCT was by Lewis *et al.*,[105,106] and examined the effect of another Spanish intervention called the Children's Epilepsy Programme. This intervention taught children and parents about seizures, living with epilepsy, and communication. Children and parents separately attended four 1.5-hour group sessions and met together at the end of each session to share learning. At follow-up at 5 months, children in the Children's Epilepsy Programme arm had significantly improved epilepsy first aid knowledge compared with children in the control arm.[105] Their parents also showed significantly greater reductions in anxiety than parents in the control arm.[106]

That training in self-care is associated with reduced service utilisation in the paediatric epilepsy population, without compromising patient outcome, concords with the larger, higher-quality evidence base on interventions to reduce ED use by children with asthma, which is another chronic, relapsing condition.[88,89,107] Boyd *et al.*,[89] for example, completed a Cochrane review of 17 RCTs of educational interventions for children (and their parents) at risk of asthma-related ED attendances. Data from > 3000 children who presented to an ED for acute exacerbations and were then followed for an average of 10 months were included. Educative interventions led to a 37% reduction in the relative

risk of reattendance at an ED in the treatment arm compared with the control arm, and a 21% reduction in the relative risk of subsequent hospital admission in the treatment arm compared with the control arm.

Conclusions from trials regarding the ability of self-management interventions to elicit behaviour change in PWE do, however, need to be tempered, because most trials have been found to be of low methodological quality.[108–110] Such trials are at a higher risk of bias and potentially overestimate effects (see Savovic *et al.*).[111] In Helgeson *et al.*'s[100] trial of the Seizures and Epilepsy Education programme, for instance, no information was provided regarding random sequence generation or allocation concealment, only 38% of those randomised to the intervention completed it and outcome assessments were not blinded.[110]

Development of the SAFE intervention

On the basis of the evidence so far presented, we hypothesised that PWE who frequently visit ED for epilepsy (here operationalised as two or more visits in the previous year) might benefit from an intervention that improves their own and their SOs' confidence and ability in managing seizures and empowers them to be able to tell others from their wider support networks about how to help if a seizure occurs. In the absence of an existing intervention it was necessary to develop one. This was done by adapting a broader intervention that was in existence and used by the ES for different purposes.

Offering such a programme to the target population is supported by the NHS policy of empowering and supporting people with long-term conditions to understand their own needs and self-manage them.[112–114] Indeed, the Keogh Urgent and Emergency Care Review[115] identified that better supporting people to self-care for their condition is one way that EDs could become sustainable.

Background to the existing seizure management course and its development

The ES is an English charity with a 120-year history that has assumed an important role in the voluntary sector in producing informative materials for PWE and in offering epilepsy training for different audiences (see www.epilepsysociety.org.uk/training-courses-epilepsy#.XSR5AutKj3g; accessed 27 August, 2019). In 2012–13, > 2000 people attended ES training courses (Joanne Fox, Learning and Development Manager, ES, 2014, personal communication). Of relevance here was their training course entitled 'Epilepsy awareness and seizure management', which they had been offering since 1998 to a fee-paying audience. Recipients included teachers, health and social care staff, PWE and SOs. The course was developed iteratively, with the involvement of neurologists, psychologists and social workers.

The course was delivered by a single educational facilitator. To deliver a course, a facilitator needed to follow a training programme developed by the ES, and a quality assurance component of ongoing internal assessment promoted consistency in delivery. The professional background of facilitators was not fixed; although they did require experience of working with PWE. Facilitators were typically people with a nursing or social care background.

Although not formally evaluated, the course was considered of interest because one of its aims was to increase recipients' confidence in seizure management, emphasising how most seizures are self-limiting, and providing a practical understanding of when seizures do and do not require emergency treatment.

Michie *et al.*'s[116] Affordability, Practicality, Effectiveness and cost-effectiveness, Acceptability, Side-effects/safety and Equity (APEASE) framework, which is intended to help guide choices about intervention development and selection for evaluation, emphasises the importance of considering, from the outset, issues such as the affordability and practicability of an intervention to ensure that the intervention is positioned to achieve its intended outcome once rolled out. With this in mind, what was also considered advantageous about the ES's course was that its delivery did not depend solely on those with specialist training in epilepsy. The UK has fewer neurologists per head than other developed nations[117,118] and only ≈ 55% of its acute trusts have access to an epilepsy nurse specialist.[119,120] Therefore, a care model that depends solely on such people may not be sustainable and generalisable.

The course in its original form

The ES's course was delivered to groups of 10–20 people. It lasted ≈ 3 hours, with breaks included. Educational aims for course recipients are specified and outlined in *Table 1*. Materials for the course included slides, professionally produced video clips of seizure types and first aid and additional information booklets on topics such as risk management and emergency medication. An information pack provided participants with a permanent record of the material and included space for notes to promote active processing of material as well as participation.

The intention was for learning to be elicited rather than taught, with the behaviour of the educational facilitator seeking to promote a non-didactic approach. Course participants were encouraged to share experiences and ask questions. To some extent there is therefore meant to be tailoring of the information that is presented so that it aligns with the needs of the group being taught (i.e. is patient centred). This, and that the course consists of a number of interacting components that may act both independently and interdependently, means that it is what the Medical Research Council refers to as a 'complex intervention'.[121,122]

Justification for developing seizure management training: a policy and service user response

The ES course is not informed by detailed theoretical modelling or a clear behaviour change model. Having reviewed and observed the intervention, our multidisciplinary research team nevertheless identified several ways by which receipt of the intervention (or a suitable adaption) could plausibly support PWE to make fewer ED attendances and improve patient and SO outcomes. These are detailed in full in *Appendix 1*. In brief, it was considered that it might increase patients' and SOs' practical understanding of seizure management, increase their knowledge of how to make appropriate care and lifestyle decisions (including the need for ED attendance) and reduce fears about risk, thereby increasing self-confidence and empowerment.

Importantly, the aims of the programme also broadly aligned with what PWE and their SOs had generally said they wanted and how they wanted to receive it. For example, studies consistently show that PWE and their SOs want more information about living with epilepsy.[27,31,123–129]

Adapting SAFE

To maximise acceptability, benefit and behaviour change potential, it was recognised that the ES's course would probably require adaptation for the target audience. To this end, the ES agreed for their course to form the basis of a new, adapted course, entitled SAFE, for PWE who frequently attend EDs and their SOs. To identify the changes required we utilised a collaborative framework underpinned by a philosophy of experience-based co-design.[130] This is an approach to improving health-care services that combines participatory and user experience design and processes to bring about quality improvements in health care.[130]

TABLE 1 Epilepsy training materials

Scope	Content
• Aim: to provide practical understanding of seizure management • Audience: broad based, including teachers, patients, care home staff • Time frame: single 3-hour session • Delivery: one educational facilitator with knowledge of epilepsy • Format: group (10–20 participants) • Style: interactive • Materials: standardised slides, videos, information booklet	• What is epilepsy? • Causes and triggers • Diagnosis • Seizure types • Potential post-seizure symptoms • Management • When to call an ambulance • Recovery position • Status epilepticus • Treatment, medication, side effects • Risk management • Accessing support and information

The need for a pilot randomised controlled trial of the SAFE intervention

Having adapted the ES's course, it would be necessary to evaluate SAFE's efficacy to determine whether or not its use in routine practice was appropriate. A definitive RCT is the most reliable methodology for determining efficacy, including of complex interventions. However, RCTs can be costly and time-consuming, especially when the trial is evaluating change in health-care service contact and when the follow-up period needs to be reasonably long. Recruitment of participants for RCTs is often slower or more difficult than expected, thus jeopardising the ability of the trial to answer its intended research question. For example, only 56% of the trials funded between 2004 and 2016 by the NIHR's Health Technology Assessment programme met their final recruitment target.[131] Before proceeding to a definitive RCT, the expenditure therefore needs to be justified, the trial deemed feasible and its design optimised.[132]

Because the adapted intervention was new and the target population not studied to a great extent, important process, management, resource and scientific uncertainties existed concerning the feasibility and optimal design of a full RCT of SAFE. The uncertainties were as follows:

- No estimates of likely recruitment, consent and follow-up rates for a definitive trial were available.
- Acceptability of randomisation to participants was unknown.
- Annual rate of ED visits in the TAU arm and the likely dispersion parameter were unknown.
- It was unclear whether or not SAFE could be delivered as intended in a trial context (fidelity).
- The resources/costs required to deliver SAFE in a trial context were unclear.
- Estimates of the effect of SAFE on primary and secondary outcome measures and their precision were lacking.

For these reasons, and informed by Lancaster *et al.*'s[133] guidance, an external pilot RCT was considered appropriate. Resembling a full RCT in many respects, such a pilot would allow us to resolve the above uncertainties and permit an informed decision to be made about whether or not and how to proceed to a definitive trial. In advance of the pilot we specified two criteria against which we would primarily judge the pilot to help evaluate the feasibility of a definitive trial:

1. At least 20% of eligible patients need to agree to participate in the pilot RCT. This was based on results from previous evaluations of self-management interventions, including the diabetes programmes that have since been commissioned by the NHS. A participant uptake rate of $< 20\%$ was deemed to raise significant concerns regarding external validity and could have implications for trial duration, recruitment centres required and feasibility.
2. Twelve-month primary outcome data need to be secured for at least 75% of participants in the pilot RCT. This figure was based on results from previous evaluations of self-management interventions that reported rates of 70–80%.[109,110,134]

Depending on the results from the pilot, one of the following judgements, based on Thabane *et al.*'s[132] decision framework, would be made regarding the feasibility of a definitive trial:

- stop – the main study is not feasible
- continue, but modify the protocol (feasible with modifications)
- continue without modifications, but monitor closely (feasible with close monitoring)
- continue without modification (feasible as it is).

Chapter 2 Part A: intervention development

Introduction

Part A sought to develop SAFE for both PWE who frequently visit hospital EDs and their SOs. To do this, the ES's existing course 'Epilepsy awareness and seizure management' was adapted and its behaviour change potential optimised.

Many self-management interventions to date have been derived from limited expert opinion and have not involved PWE and other stakeholders in the planning process.[129] By contrast, and to help ensure maximum benefit and acceptability to users, we used an experience-based co-design approach.[130] Such an approach allows researchers to work collaboratively with people from the target population to identify their specific learning needs, clarify their delivery preferences and adapt the intervention to match these.

We were mindful of the need for SAFE to be viable for delivery within the NHS. [112–114] Examples abound of the importance of ensuring that any new intervention is supported by those who will be asked to ultimately refer their patients to it, deliver it or allocate resources to it, including in the context of epilepsy.[135] Therefore, representatives from different key professional bodies involved in the support of PWE were also consulted as part of our co-design approach.

Methods

The co-design process used comprised three iterative stages, namely (1) qualitative interviews with health-care professionals about the existing intervention, (2) optimisation of its behaviour change potential and (3) focus group (FG) discussions with service users. The process is outlined in *Figure 1*.

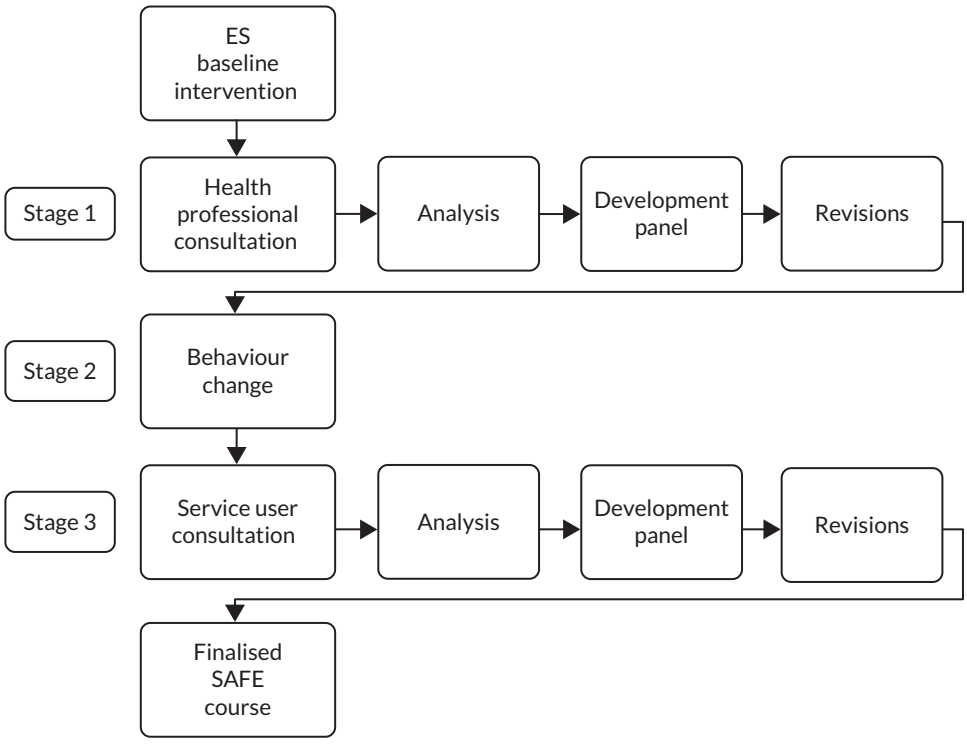

FIGURE 1 Intervention development process.

Participant settings and samples

Stage 1: recruitment of health-care professional representatives

Different health disciplines can be involved in the care of PWE. Some patients will identify a general practitioner (GP) as the main provider of their ambulatory care whereas others will identify a specialist, such as a neurologist or epilepsy. The voluntary sector is also an important support structure for many PWE. When someone seeks emergency care for a seizure, other parts of the health system come into contact with PWE, including paramedics and ED staff. All parties were considered as being positioned to be able to offer insights into the support needs of PWE who attend for seizures. We therefore chose to adopt purposeful sampling for the identification and selection of information-rich cases[136] from the main parts of the care pathways encountered by PWE. This involved identifying and selecting individuals who were especially knowledgeable about or experienced with the phenomenon of interest.[137] In addition to knowledge and experience, participant availability and willingness to participate were key considerations.[138,139]

Seven professional organisations (*Table 2*) identified a representative potentially interested in participating. Each representative was sent a participant information sheet (see *Appendix 2*), and those taking part signed a consent form. Interviews were conducted by a qualitative researcher (Adwoa Hughes-Morley; see *Acknowledgements*) and took place at a time and in a format convenient for the representative, be that via telephone, Skype™ (Microsoft Corporation, Redmond, WA, USA) or face to face at the representative's office. Each representative was offered a consultancy fee of £200.

Ultimately, a consultative group comprising nine health-care professionals from seven different disciplines was established to provide feedback on the content of the ES course. This group included two consultant neurologists (one with a specialist interest in epilepsy), two consultants in emergency medicine, a consultant paramedic, a epilepsy nurse specialist, a GP with a specialist interest in epilepsy, a service commissioner with a health-care background and an educational representative from an epilepsy charity other than the ES.

TABLE 2 Health-care professional consultation: groups supporting PWE

Group	Details
• International League Against Epilepsy – British branch	• URL: https://ilaebritish.org.uk (accessed 11 June 2020). London, UK
• Royal College of Emergency Medicine	• URL: www.rcem.ac.uk (accessed 11 June 2020). London, UK
• GPs with a specialist interest in epilepsy	• None
• Epilepsy Nurses Association	• URL: www.esna-online.org.uk (accessed 11 June 2020)
• North West Ambulance Service NHS Trust	• URL: www.nwas.nhs.uk (accessed 11 June 2020). Bolton, UK
• Cheshire Merseyside Strategic Clinical Networks (commissioning representative)	• Bromborough, UK
• SUDEP Action (formerly Epilepsy Bereaved) user group	• URL: https://sudep.org (accessed 11 June 2020). Wantage, UK

Stage 3: recruitment of service user representatives

Feedback on the intervention was obtained from a purposive sample of service user representatives. PWE were eligible to participate in SAFE training if they met the following inclusion criteria:

- established diagnosis of epilepsy (≥ 1 year)
- currently prescribed antiepileptic drug(s)
- age ≥ 16 years (no upper age limit)
- visited an ED for epilepsy at least once in the past 2 years (as reported by the patient)
- living in the north-west area of England
- able to provide informed consent and participate in SAFE course in English.

People with epilepsy were excluded from participating in SAFE training if they reported:

- acute symptomatic seizures
- severe current psychiatric disorders
- life-threatening medical illness.

Patient participants could take part with or without a SO. SOs with the following characteristics were eligible to participate in SAFE training:

- a SO to the patient (e.g. family member, friend) who the patient identifies as providing informal support
- age ≥ 16 years (no upper age limit)
- living in the north-west area of England
- able to provide informed consent and participate in SAFE course in English.

Significant others were excluded from participating in SAFE training if they reported:

- severe current psychiatric disorders (e.g. acute psychosis)
- life-threatening medical illness.

The service user representatives were identified via adverts circulated (via newsletters and websites and at meetings) to the affiliates of user groups, including the Mersey Region Epilepsy Association (Liverpool, UK), the Brain & Spine Foundation (London, UK), NeuroSupport Services Ltd (Nottingham, UK) and the ES. This approach enabled the recruitment of 'experts', defined as informed individuals with knowledge or experience of a specific subject.[140,141] Eligible patients and SOs interested in taking part were sent a participant information sheet (see *Appendix 3*) and those taking part signed a consent form.

A total of 23 service user representatives were ultimately recruited, comprised 13 PWE (seven men and six women) and 10 SOs (four men and six women). Each received a £10 shopping voucher.

Intervention development panel members

The process was overseen by an intervention development panel. The panel considered and discussed the findings from the interviews and FGs and made required adaptations to the intervention. The panel included patient and SO representatives [Mike Perry (MP) and Linda Perry (LP)], a psychologist (AN), a neurologist (LR), a medical sociologist (MM), a research nurse with specialist qualitative research training (DS) and a representative from the ES's training division. Patient and SO representatives were active in all aspects of the decision-making and were reimbursed in line with guidance.[142]

Developing the intervention

Stage 1: consultation with health-care professional representatives

Consensus exists regarding what constitutes appropriate seizure first aid.[143–145] Thus, the purpose of this stage was to interview representatives from the main professional bodies caring for PWE to ascertain whether or not the medical information presented by the programme was correct and whether or not SAFE could be an intervention they could, in the future, support. It was considered important to seek feedback from professionals in the first instance to prevent PWE (and SOs) being exposed to possibly incorrect information. Moreover, it would allow us to identify from the start what sort of seizure first aid intervention was considered feasible for delivery in the context of the NHS. The health-care professional representatives each conducted a baseline document and audiovisual review of the course materials for the ES's existing intervention.

In advance of their interviews, each representative was provided with the course materials. Approximately 2 weeks later, data from each of the nine representatives were collected via audio-recorded semistructured interviews. A topic guide was developed to reflect the intended purpose of the stage and on the basis of the literature (see *Appendix 4*). It was refined through the iterative process of the interviews.[146,147] The exact questions varied depending on the representative's area of expertise, but all health-care professional interviews included key discussions on:

- identifying inaccuracies in the content of the existing ES programme
- likes/dislikes and the appropriateness of the current content and delivery
- suggestions about how to make the programme more helpful
- how SAFE might be best rolled out in the NHS if a future trial found it to be effective.

Stage 2: optimisation of the intervention's behaviour change potential

A significant component of the ES's intervention consisted of health-related information provision. It was anticipated that the provision of such information could reassure service users and increase seizure management confidence and competence. However, for some PWE the information might actually highlight that their prior use of ED conflicted with medical guidance. From a psychological perspective, this could be construed as a threat to self-integrity. As a consequence, these people might be at risk of rejecting or denigrating the information provided by the SAFE intervention, which may compromise its ability to elicit behaviour change. According to self-affirmation theory,[148] people are fundamentally motivated to preserve a positive, moral and adaptive self-image and to maintain self-integrity. Consequently, health messages that threaten one's sense of self-image can be subject to defensive processing (e.g. motivated scepticism, unrealistic optimism).[149]

To mitigate against this and maximise the behaviour change potential of SAFE, the intervention development panel decided to introduce a self-affirmation exercise, namely Reed and Aspinwall's[150] kindness questionnaire, which individuals would complete at the start of SAFE training. The rationale was that evidence indicates that having a person complete an exercise such as recalling one's acts of previous kindness prior to receipt of health risk messages reduces resistance to threatening or dissonant health risk information. This is because theory indicates that a person's self-image can be maintained by self-affirming in one domain (e.g. recalling one's acts of kindness) even if one is being threatened in another domain (e.g. health), because people can defend their global sense of self-worth rather than (for example) against the threat directly attributable to health risks.[151,152]

The kindness questionnaire was considered ideal because it is brief (taking $\approx$ 5 minutes to complete) and effective[150,153] and does not need to be delivered by specialists. It consists of 10 questions that participants work through by themselves, including 'Have you ever been concerned with the happiness of another person?' and 'Have you ever forgiven another person when they have hurt you?', with yes/no response options. The intention was that PWE and SOs would each complete it at the start of SAFE.

Their questionnaires were not to be collected by any member of the intervention team and the participant would not be asked how they answered.

Stage 3: consultation with service user representatives

To allow service user representatives to critically feed back on SAFE, two practice courses were run in November 2015 using the intervention that resulted from the first two stages. These were followed by FG discussions.

The courses took place in a local hospital's education centre and were delivered on weekdays to groups of ≈ 10 patient–SO dyads. A facilitator from the ES (Juliet Bransgrove; see *Acknowledgements*), who was an epilepsy nurse specialist with experience of delivering the ES's course, delivered the courses. She underwent a period of familiarisation with the adapted intervention by reviewing the new materials and a trainers' manual (see *Report Supplementary Material 1*) and meeting the intervention development panel.

The FGs, which lasted ≈ 60 minutes each, were conducted by a trained qualitative researcher (DS) to explore participant views. The researcher observed each course and recorded impressions of participants' engagement with the materials, the group and the facilitator. A topic guide (see *Appendix 5*) reflecting the discrete sections of the course guided the FGs. Participants were asked about issues related to the course content and delivery as well as for views around its perceived strengths and barriers to its successful implementation.

Analytic process

The interviews, practice course events and FGs were recorded (with participants' consent) and transcribed verbatim. Transcripts were checked for accuracy by the researcher (DS) who conducted the data collection. A comprehensive inductive and deductive approach was used, with NVivo version 10 (QSR International, Warrington, UK)[154] being used to provide a transparent account of the work. Nodes (codes) were created to mark relevant concepts and topics in the text documents. Lower-level nodes were then grouped into themes. An account of the process of analysis was logged in the memos attached to categories and interview and FG documents, including the questions used to interrogate the data, and thoughts and decisions about what themes to focus on. These capabilities and the associated process fit with the iterative goals of the development stages of the training intervention. Direct quotations are provided in the text as a means to verify interpretation and illustrate themes.

Results

Health-care professionals

Analysis of health-care professionals' responses highlighted three key themes, namely (1) initial impressions, (2) areas of intervention in need of revision to promote effective participation and (3) course delivery.

Initial impressions

There was consensus on the need for such an intervention and its potential for cost-effectiveness. As one representative noted:

> *[I]t will be a powerful tool to upskill and reassure [. . .] The clearer they are about what constitutes that person's normal epileptic fit and what maybe a bit unusual, the more [. . .] appropriate the response the better their [. . .] overall experience, privacy, dignity and everything to follow [. . .] [I]t's a fairly easy case to make for the commissioners [. . .] Resources directed by commissioners to pay for this really unnecessary attendance could be redirected [. . .] win–win.*
>
> *ED consultant*

The existing intervention was seen to provide a useful starting point for adaption and professionals liked the videos and associated information booklets:

> *There's a solid foundation in there which you can build on to then create the course to make sure it reaches the kind of outcomes that you are after [. . .] It's just making sure that it hits all those objectives along the way.*
>
> *User group representative*

The practical challenges of hosting a group-based course were highlighted by many; it was thought that 'getting people together may be a difficulty' (epilepsy specialist nurse) that would require careful consideration, especially in relation to 'distance and timing' (epilepsy specialist nurse). It was important, therefore, to 'think about local delivery and minimising travel time' (epilepsy nurse specialist).

It was also felt that substantial changes were needed to make the intervention appropriate for its new audience and to achieve the aim of attenuating unnecessary/avoidable ED use.

Areas of intervention in need of revision

It was deemed important to better emphasise the benefits of the course to PWE and SOs with a more focused and 'clear message' at the start on the need or not for ED attendance after a seizure. Language level was highlighted as an area that required revision in line with the average UK literacy level. There were also suggestions, as presented below, to revise the style of presentation so that it was less for people who might be involved in epilepsy because of their profession:

> *[I]t's written in quite a wordy way and probably a few more pictures and a few less words [. . .] would be better. This is probably a very good presentation to new health-care professionals [. . .] but probably not great for people that [. . .] have no training whatsoever.*
>
> *Consultant paramedic*

It was considered that a behavioural change focus (emergency medicine consultant 1) should be brought to the fore and that the benefits to the participant and SO of avoiding unnecessary ED visits should be emphasised. As explained by the GP representative:

> *It's about helping people manage their epilepsy better. What will the course do for you? What can you get out of the course? [. . .] The course should focus on behavioural change, but the impression should not be given that the focus is about reducing A&E [accident and emergency department] admissions – that would be counterproductive. Rather, it is about highlighting the benefits, such as better management will reduce inconvenience in having to go to A&E.*
>
> *GP*

A recurring theme was the need to better elicit and address patient concerns and that patient and SO participation should be promoted through more interactive exercises, the inviting of questions and the discussing of fears, because this was when 'true education happens'. This was summarised by one representative:

> *[S]eizure management, what you should do and what you wouldn't do [. . .] I'd make that part interactive [. . .] get them to tell you, get their opinion and their views before and then you show them what they probably should do afterwards but find out. Because you'll probably [. . .] challenge them [. . .] that's the point where you really get them I think.*
>
> *Consultant neurologist*

A number of participants pointed out that, when seizures happen in public places, the decision to seek emergency care is not necessarily the patient's or their SO's. Therefore, it was recommended that the

intervention should support patients to develop and carry with them personalised care plans on paper or on their smartphones, which could be used inform decision-making by paramedics:

> *[I]f we [the ambulance service] tip up and we don't know anything about you we are taking you to hospital [. . .] We're tipping up to what we consider to be a first-time fit until proven otherwise [. . .] Have a care plan written or something on you that says 'I'm an epileptic and this is what happens to me normally'.*
>
> *Consultant paramedic*

Course delivery

Participants observed that, to make the course suitable for delivery in the NHS and to promote quality and consistency among trainers, the intervention should become fully standardised and a trainer's manual, including recommended times for each topic/activity, developed.

With respect to attributes and skills of an ideal facilitator to deliver the course, some identified epilepsy nurse specialists. However, others felt that the epilepsy voluntary sector was well developed and, therefore, related commissioning organisations could help avoid shortfalls where specialist staff were not available. It was considered that the following should be true in any circumstance:

> *The facilitator is someone who should have knowledge of epilepsy and be good at leading groups. They need the ability to keep the course on track and to time, especially when participants may want to talk a lot!*
>
> *Epilepsy nurse specialist*

Changes made by intervention development panel to create version 1.1

There was agreement in the intervention development panel that the intervention's content needed to be revised to be better directed towards the goal of attenuating unnecessary ED use. Therefore, the aims for the new intervention were specified as helping participants to:

- feel more confident to manage their seizures/the seizures of someone they know
- know how to tell others how to help
- know some things that may reduce the chances of a seizure
- know some things that may reduce the chances of injury from a seizure.

There was also agreement in the intervention development panel that more interactive activities were needed. Interactivity was considered important as it permits participants to share and learn from each other, can foster a sense of empowerment and means that participants ask questions and seek clarification to ensure that the intervention is tailored to their needs. As part of the discussion, evidence from the diabetes self-management literature was reflected on, which suggests that interaction between participants and the facilitator can be important in promoting behaviour change. Skinner *et al.*[155] calculated the ratio of facilitator talk to participant talk during a group-based education intervention for diabetes and found that lower facilitator talk ratios predicted greater improvements in participants' metabolic control and beliefs about diabetes.

In line with these requirements, Adam Noble and Darlene Snape revised the intervention, generating new presentation materials, introducing new content and generating a training manual for facilitators. In doing this, attention was given to presenting information in an easy-to-understand style, with feedback from the 'plain English' section of the ES's information department being obtained. *Table 3* details the changes made to the ES's intervention at this stage.

To promote more interaction, four new activities were introduced. One involved practising the recovery position; another required subgroups to find answers to different questions concerning seizure first aid from among a group of acetates and to present these. This was designed to identify participant beliefs and fears and for these to be discussed. The final two activities centred on case studies. These involved participants being read illustrated stories of patients and asked to consider what

TABLE 3 Content of original course and revisions made following feedback

Original course: version 1.0				Post stage 1: version 1.1 (post professional consultation and discussion by intervention development panel; subsequently presented to users)				Post stage 2: version 1.2 (post pilot training sessions, user FGs and discussion by intervention development panel; delivered as the intervention in study phase B pilot RCT)			
Title											
Epilepsy awareness and seizure management				Epilepsy Seizure First Aid Training				Managing seizures: epilepsy first aid training, information and support			
Duration (hours)											
3				3				4			
Materials											
Slide projector, flipchart, video, information packs (including wallet-sized first aid instructions cards, paper epilepsy ID cards, contact details for further information) and certificates of attendance				Slide projector, flipchart, video, information packs (including wallet-sized first aid instructions cards, paper epilepsy ID cards, instructions for IDs on telephone, contact details for further information) and certificates of attendance				Slide projector, flipchart, video, information packs (including wallet-sized first aid instructions cards, paper epilepsy ID cards, instructions for IDs on telephone, contact details for further information, web address for copies of the course materials) and certificates of attendance			
Order	**Learning topic**	**Learning activity**	**Minutes allotted**	**Order**	**Topics**	**Learning activity**	**Minutes allotted**	**Order**	**Topics**	**Learning activity**	**Minutes allotted**
1	Aim of this session	Slide	–	1	Welcome	Slide	5	1	Welcome	Slide	5
2	Objectives	Slide	–	2	Taking on information (kindness questionnaire)	Interactive	10	2	Goals of this course	Slide	2
3	Session outline	Slide	–	3	Goals of this course	Slide	2	3	What would you like from today?	Interactive	20
4	Myth or truth?	Interactive	–	4	What would you like from today?	Interactive	5	4	True or false?	Interactive	12
5	What is epilepsy?	Slide	–	5	True or false?	Interactive	8	5	Taking on information (kindness questionnaire)	Interactive	10
6	The brain …	Slide	–	6	Epilepsy, seizures and how the brain works	Video	10	6	Epilepsy, seizures and how the brain works	Video	10
7	Lobes of the brain	Slide	–	7	First aid for convulsive seizures	Interactive	10	7	First aid for convulsive seizures	Interactive	10

Order	Learning topic	Learning activity	Minutes allotted	Order	Topics	Learning activity	Minutes allotted	Order	Topics	Learning activity	Minutes allotted
8	How the brain works …	Slide	–	8	What can you do to help someone during a seizure?	Slide	5	8	What can you do to help someone during a seizure?	Slide	5
9	Seizures happen when …	Slide	–	9	What not to do during a seizure	Slide	5	9	What not to do during a seizure	Slide	5
10	Seizures are …	Slide	–	10	What to do after the seizure has stopped	Slide	5	10	What to do after the seizure has stopped	Slide	5
11	Possible causes of epilepsy	Slide	–	11	When to call an ambulance	Slide	10	11	Questions or comments?	Interactive	10
12	Diagnosis	Slide	–	12	Questions or comments?	Interactive	5	12	Post-seizure states	Slide	15
13	Triggers	Slide	–	13	Refreshment break	Networking	10	13	Injuries	Slide	2
14	Seizure types and first aid	Video	15	14	Recovery position	Slide	2	14	When to call an ambulance	Slide	10
15	Seizure management	Interactive	–	15	Recovery position	Video	2	15	Questions or comments?	Slide	10
16	Recovery position	Slide	–	16	Let's practice the recovery position	Interactive	8	16	Refreshment break	Networking	10
17	Maintain airway	Slide	–	17	Questions or comments?	Interactive	5	17	Recovery position	Slide	2
18	When to call an ambulance?	Slide	–	18	Who needs to know how to help?	Interactive	3	18	Recovery position	Video	2
19	Most seizures are …	Slide	–	19	What they need to know and why	Slide	5	19	Let's practise the recovery position	Interactive	15
20	Status epilepticus	Slide	–	20	How to get this information to them: family, friends and work colleagues	Slide	5	20	Questions or comments?	Interactive	5

continued

TABLE 3 Content of original course and revisions made following feedback (*continued*)

Order	Learning topic	Learning activity	Minutes allotted	Order	Topics	Learning activity	Minutes allotted	Order	Topics	Learning activity	Minutes allotted
21	Sudden unexpected death in epilepsy	Slide	–	21	How to get this information to them: members of the public and health workers	Slide	5	21	Who needs to know how to help?	Interactive	5
22	Treatment with drugs	Slide	–	22	Questions or comments?	Interactive	5	22	What they need to know and why	Slide	5
23	Medications	Slide	–	23	Refreshment break	Networking	10	23	How to get this information to them: family, friends and work	Slide	5
24	Medication	Slide	–	24	Personal stories: introduction	Slide	2	24	How to get this information to them: members of the public and health workers	Slide	5
25	Possible side effects of medications	Slide	–	25	Ben's story	Slide	5	25	Questions or comments?	Interactive	5
26	Other possible treatments	Slide	–	26	How to change what happened to Ben (carrying medical ID; triggers)	Interactive	5	26	Refreshment break	Networking	5
27	Minimising risk	Slide	–	27	Triggers	Slide	5	27	Personal stories: introduction	Slide	2
28	Keeping safe	Slide	–	28	Knowing your triggers	Slide	5	28	Ben's story	Slide	6
29	Supporting the 'whole person'	Slide	–	29	Some ways of dealing with triggers	Slide	10	29	How to change what happened to Ben (carrying medical ID; triggers)	Interactive	5
30	To the future …	Slide	–	30	Questions or comments?	Interactive	5	30	Triggers	Slide	5

Order	Learning topic	Learning activity	Minutes allotted	Order	Topics	Learning activity	Minutes allotted	Order	Topics	Learning activity	Minutes allotted
31	Further sources of information	Slide	-	31	Sandra's story	Slide	6	31	Knowing your triggers	Slide	4
32	Any questions?	Interactive	-	32	How to change what happened to Sandra (warning signs; home safety)	Interactive	5	32	Some ways of dealing with triggers	Slide	4
33	Certificates of attendance	Slide	-	33	Main points to remember if you have epilepsy	Slide	5	33	Sandra's story	Slide	6
34					Main points to remember if you know someone with epilepsy	Slide	5	34	How to change what happened to Sandra (warning signs; home safety)	Interactive	2

ID, identification.

things the patient in the story might have done to have achieved a better outcome. The carrying of epilepsy identification was one way in which the outcome of one of the stories could have been changed.

It was estimated that, in the revised intervention, 114 minutes (47.5%) was dedicated to interactional/networking elements, 114 minutes (47.5%) to slides and 12 minutes (5%) to video.

Service users

Having received version 1.1 of the adapted course, three key themes emerged from the analysis of service users' responses. These included 'the need to know', 'barriers to and drivers of effective participation in training' and 'course delivery'.

The need to know

All patient and SO participants identified the need for such a course, with lack of prior support in self-management as a recurring topic of discussion. For example, participants explained as follows:

> *It can be quite overwhelming I think for partners. It's like 'all on their shoulders' what happens. I think your carer needs a lot of support too.*
>
> *Patient 3, male (M), FG 1*

> *The consultants they just presume that you know [about epilepsy] [. . .] but for all the years he got put on tablet or tablets [. . .] you didn't see or hear any of this [information presented on the course]. So it's suddenly all of an eye-opener and talking here you realise we are not on our own.*
>
> *SO 1, female (F), FG 1*

Similarly, another SO noted:

> *I always think of epilepsy as the poor relation [. . .] not much on TV or adverts about epilepsy support [. . .]. A course like this helps to develop that sense of support as well as improve knowledge.*
>
> *SO 2, M, FG1*

Concerns expressed by SOs centred on the 'need to know I'm doing the right thing' (SO 4, F, FG 1). PWE expressed concerns about disclosure and how best to tell others around them how they should help if a seizure happened; they wanted information and advice on how best to manage this. Overall, service user participants described three areas of perceived need: knowledge acquisition around epilepsy, emotional and/or practical support, and dealing with isolation and stigma.

Taken as a whole, the content of the revised course (version 1.1; see *Table 3*) was felt to be 'excellent' (patient 3, M, FG 2) and appropriate. Of particular importance to the users was the straightforward guidance that an ambulance was required when seizures lasted for 5 minutes or longer. This information alone was found to be helpful and reassuring, and some said that they would no longer always call immediately for an ambulance: 'I think I will wait longer [to call an ambulance] than I did before picking up the phone' (SO 3, F, FG 2); 'I will wait [to call an ambulance] rather than when he has a seizure going for the phone straight away' (SO 7, F, FG 2).

Concerns with regard to how to tell others about epilepsy and how to help if a seizure happens were expressed:

> *Like when you go somewhere you need to remember to like tell people that you have seizures.*
>
> *Patient 1, M, FG 1*

> *I need to know how best to share with others [family/friends/colleagues] the implications of having epilepsy.*
>
> *Patient 2, F, FG 1*

To this end there was consensus, for the most part, that the need to feel informed and reassured on what to do when seizures occurred had been met. Participants expressed how they had 'learned a lot' (SO 5, F, FG 1) from the session.

The balance between taught and interactive components was felt to be appropriate. The provision of information was viewed as reassuring and the opportunity to practise the recovery position was valued. As one patient asserted:

> *Watching a video would just go straight over me head, but actually putting [patient name] on the floor and putting him in the right position will help. For me that's very useful [. . .] something like that I won't forget.*
>
> *Patient 5, F, FG 1*

The training session was considered to cover more than implied by its title. Participants said that the 'wider remit' (patient 10, F, FG 2) was desirable but that a more accurate title was needed to engage future service users. 'Managing seizures: epilepsy first aid training, information and support' was identified as more suitable for the purposes of advertising.

Barriers to and drivers of effective participation in training

Service users' perceptions of barriers to and drivers of successful training were explored. One was the self-affirmation kindness questionnaire.[149] Its positioning and purpose in the session were not understood by most participants: '[. . .] just coming into the session the questionnaire seemed inappropriate' (SO 3, F, FG 1). It was also found by some to be threatening: 'It felt like a test and a bit off-putting' (SO 4, F, FG 1).

Some service users reported that another barrier was that there was 'a lot of information to take in' (patient 4, M, FG 1), and issues relating to memory difficulties were highlighted. Therefore, participants supported the use of handouts and requested an online copy of the materials that they could access and share with others.

With respect to content, important feedback from service users was that they appreciated that attention was given to the different types of seizures and how to manage them and that the focus was not simply on 'grand mal seizures' (SO 5, F, FG 1). However, they suggested that more time be given to exploring triggers and auras and to explain that not everyone has triggers, which in itself is a potential risk. It was also suggested that new sections should be included to discuss the risks associated with post-ictal states and how best to deal with them. Finally, some suggested that 'dealing with an injury as well as dealing with the seizure can be difficult' (SO 7, F, FG 2), and, therefore, information and advice on how to deal with common seizure injuries were needed.

Course delivery

The size of the group (up to 20 people) was considered to be appropriate and encouraged discussion. Indeed, peer support and a sense of feeling 'less isolated' was highlighted as a key training experience. Many patients had not previously discussed their epilepsy with people other than their immediate family members and/or health-care professionals. They valued the group format and described how they appreciated being able to meet others who were 'in the same boat' and 'realising you are not on your own with it' (patient 6, M, FG 1). One SO noted:

> *[R]eally glad I came. I think it's just being around people who know exactly, exactly how you feel and that's why this should have been put on a long, long time ago.*
>
> *SO 1, F, FG 1*

In terms of who would be best to facilitate the course, many felt that it should be a health-care professional because they believed that this would make the course 'credible' (patient 8, F, FG 2) and promote uptake. Others, however, argued that it could be facilitated by a representative from a user group because what was most important was that the trainer was knowledgeable and empathetic and had the skills to facilitate discussions. Either way, it was argued that standardised training for the facilitators was important.

Changes made by the intervention development panel to create version 1.2

The user feedback led to a refashioning of a number of details in the way that SAFE was to be delivered (as version 1.2; see *Table 3*). To increase the acceptability to users of the self-affirmation kindness questionnaire, it was agreed that this would not be introduced to participants until ≈ 30 minutes into the session and would follow the 'icebreaker' rather than being introduced immediately.

Given that the main aim of SAFE was to help patients and SOs manage uncomplicated seizures, the panel revised SAFE so that information on managing common post-ictal states was included. However, for the same reason, training PWE and SOs in dealing with seizure injuries as requested was deemed to be beyond SAFE's scope. Therefore, SAFE was modified to simply acknowledge the possibility of injuries and direct participants to external resources on this.

The length of version 1.2 of SAFE was extended from ≈ 3 to ≈ 4 hours. The increased duration meant that more time could be allocated to the interactive elements of SAFE. Finally, a password-protected website (www.seizurefirstaid.org.uk/Intervention/; accessed 15 June 2020) that provided a copy of SAFE's content was developed in an effort to mitigate potential memory difficulties in the target population. It also provided a means by which participants could share SAFE's content with others in their social network.

Discussion

The focus of part A was to develop an epilepsy first aid training intervention that met the needs and preferences of both PWE who frequently visit hospital EDs and their SOs. To promote adequate development and piloting[156] we worked collaboratively with service users and other key stakeholders. This activity was underpinned by the Medical Research Council's complex intervention guidance.[156] The process enabled us to access the unique perspectives of service users and health-care professionals. Clear, tangible changes to the ES's course were made in response to the feedback received; the developed SAFE intervention is substantially different in content and form. By making these changes, the acceptability of SAFE in the target population has been increased. Stakeholder collaboration has maximised SAFE's potential benefit and positioned it well for sustained use in the NHS, should this ultimately prove warranted. We described the process we followed and detailed the content of the finalised intervention that will be used within the pilot trial. Such an account is rare, with outcome papers frequently being criticised for not providing readers with sufficient information to interpret trial results.[157]

Chapter 3 Part B: pilot RCT – methods

Introduction

Part B of this project was an external pilot RCT of SAFE plus TAU versus TAU only. It sought to:

- estimate the eligibility rate
- estimate the consent rate
- estimate the recruitment rate
- estimate the retention rate
- determine the acceptability of randomisation to participants
- determine the speed of recruitment
- estimate completion rates of study assessment tools
- estimate rates of unblinding
- estimate the annual rate of ED visits in the TAU arm and the likely dispersion parameter
- generate summary statistics to measure the effect of SAFE on the proposed primary and secondary outcome measures for a future definitive trial and the precision of such estimates at the post-treatment time points
- determine the feasibility of measuring the primary outcome measure (ED use) by means of routine data.

Design

The trial was as a multicentre, parallel-arm pilot RCT. Participants were PWE with or without a SO. PWE (and their SO if participating with one) were randomised at an intervention-to-control ratio of 1 : 1 and followed up for 12 months. The intervention arm received TAU and was offered the SAFE course and the control arm received TAU. To maximise recruitment, the TAU arm was offered the intervention once all scheduled 12-month follow-up assessments had been completed. The study also contained an evaluation of the fidelity with which SAFE was delivered (see *Chapter 5*) and an economic evaluation of the cost of delivering it (see *Chapter 7*). The trial's design and the intended flow of participants are shown in *Figure 2*.

The trial protocol received the favourable opinion of the National Research Ethics Service Committee North West — Liverpool East (reference: 15/NW/0225) and Health Research Authority (reference: 166241). Its sponsor was the University of Liverpool (reference: UoL001108). The trial was registered on an open access system (Current Controlled Trials ISRCTN13871327).

Trial progress and conduct was monitored by an independent Trial Steering Committee composed in line with National Institute for Health Research guidelines. In line with these oversight guidelines, a Data Monitoring and Ethics Committee was not required.

Study setting and population

Centres

Participants were retrospectively identified from the EDs of three NHS hospitals in Merseyside – namely, Aintree University Hospital, Arrowe Park Hospital and the Royal Liverpool University Hospital. Together, these EDs serve a local population of ≈ 827,000 people among whom the prevalence of adult epilepsy is 0.98%.[26] At each site, an ED consultant acted as a local principal investigator.

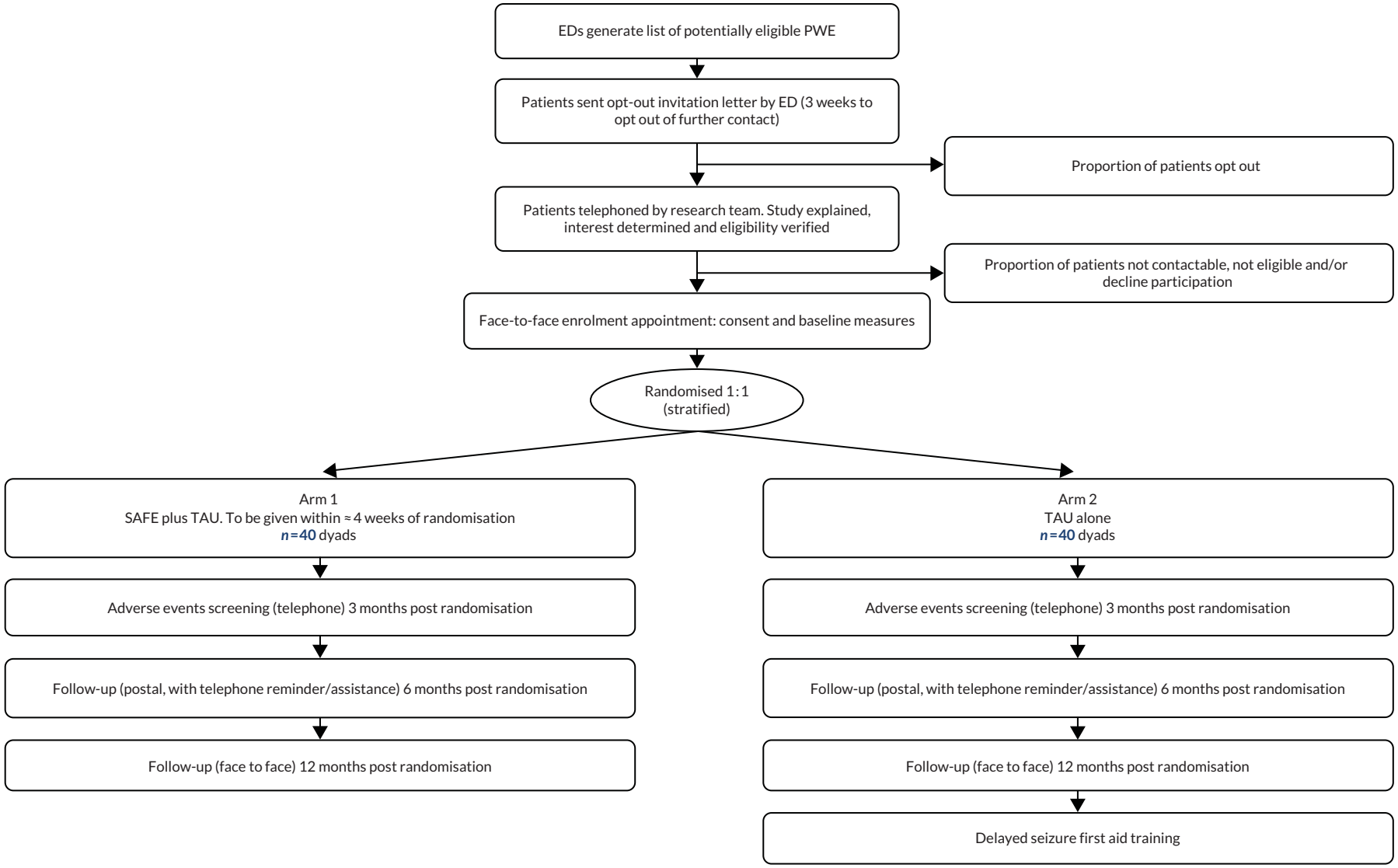

FIGURE 2 Schematic of planned design for part B of the project: trial approval and monitoring.

The EDs were selected as research sites because they would probably be similar to those sites that would be most appropriate for a definitive trial. Specifically, the EDs serve a population characterised by high levels of social deprivation,[158,159] a level of epilepsy control that has been documented to be worse than the national average and rates of emergency admissions for epilepsy that are among the highest in England (Liverpool is ranked as the ninth highest and Wirral is ranked as the twelfth highest).[41] Epilepsy control is defined here – on the basis of the *Quality and Outcomes Framework 2012–13*[160] domains – as the percentage of PWE prescribed one or more antiepileptic drugs in the local population who have been seizure free in the previous 12 months. When the trial was being designed, 70.9% of PWE from the Clinical Commissioning Group areas served by the hospitals were seizure free. The national average at the time was 75.4%.[41]

Participant inclusion criteria

Patients with the following characteristics were eligible:

- established diagnosis of epilepsy (for ≥ 1 year)
- any epilepsy syndrome and any type of focal or generalised seizures
- currently being prescribed one or more antiepileptic drugs
- aged ≥ 16 years (no upper age limit)
- visited an ED for epilepsy on two or more occasions in the previous 12 months (as reported by patient)
- living within 25 miles of any of the three ED recruitment sites
- able to provide informed consent, participate in SAFE and independently complete questionnaires in English.

Significant others with the following characteristics were eligible:

- a SO to the patient (e.g. family member, friend) whom the patient identifies as providing informal support
- aged ≥ 16 years (no upper age limit)
- living in the north-west area of England
- able to provide informed consent, participate in SAFE and independently complete questionnaires in English.

Participant exclusion criteria

Patients with the following characteristics were excluded:

- actual or suspected psychogenic non-epileptic seizures alone or in combination with epilepsy
- acute symptomatic seizures related to acute neurological illness or substance misuse (e.g. alcohol or drug induced)
- severe current psychiatric disorders (e.g. acute psychosis) or life-threatening medical illness
- enrolment in one or more other epilepsy-related non-pharmacological treatment studies.

Significant others with the following characteristics were excluded:

- severe current psychiatric disorders (e.g. acute psychosis) or life-threatening medical illness
- enrolment in one or more other epilepsy-related non-pharmacological treatment studies.

Screening

Stage 1

There is no central, 'live' system that can be accessed and searched to identify PWE who have made visits to NHS EDs in England. Well-documented challenges to information sharing between NHS services also mean that specialist services and GPs are not necessarily aware of ED attendances made by PWE for whom they care.[20,21] However, hospitals in the UK do maintain local electronic records of attendances at their EDs. For each attendance, a local record contains the patient's contact details and

a number of searchable fields, including date of attendance, patient age, home postcode, presenting complaint and, if provided, a discharge diagnosis. These attendance systems of the EDs were used to identify PWE who had attended the EDs in the last 12 months for invitation to the trial.

Searches of the local systems for PWE were completed by the business intelligence units of the hospitals. We had envisaged that an independent expert panel of neurologists and ED clinicians would determine the search criteria to be used (e.g. presentation and diagnosis codes). During study set-up it became apparent that the architecture of the systems and the coding processes at each of the sites were sufficiently different that local knowledge of the system was required to have confidence that the criteria used would allow for a sufficiently sensitive and specific search to occur. Therefore, we instead worked with the local principal investigators at each site to identify the optimal search strategy. The search terms used are detailed in *Appendix 6*.

Stage 2

The 'triage cards' of the patients captured by the searches during stage 1 were reviewed by the local principal investigator and their team to identify persons who were and were not eligible to invite. This level of detailed screening was necessary because (1) no symptom presentation is pathognomonic of epilepsy (e.g. a presentation coded as 'blackout/faint' or 'fit/seizure' could be attributable to syncope, diabetes, head injury or stroke rather than epilepsy) and (2) the discharge diagnosis field was often empty. In 2016/17, ≈ 35% of ED attendances in England were not allocated a valid primary diagnosis code.[161]

Those patients who, following review of their triage card, were considered ostensibly eligible by the local principal investigator were sent an invitation pack, which included a covering letter from the ED consultant and a patient participant information sheet (see *Appendix 7*). The letter informed the patient that, unless they opted out of further contact within 3 weeks or sent notification that they were ineligible, they would be telephoned by the research team with more information about the study. Patients could opt out by e-mail, telephone or by returning a Freepost slip. Those opting out were encouraged to detail any reasons. Those interested in taking part were asked to await contact by the research team and consider whether or not they would like to take part with a SO.

Stage 3

Interested patients were telephoned to answer questions the patient had, confirm whether or not the patient wanted to participate and verify their eligibility (including that they had made two or more ED visits for epilepsy in the last 12 months). If a person was confirmed as eligible and wanted to participate, consent in principle was taken over the telephone and the research worker arranged a baseline/enrolment appointment at which informed signed consent was to be obtained from them and from their SO if they were taking part with one.

Multiple telephone calls were attempted with patients who had not opted out. Attempts to call participants were made on different days of the week and at different times. A total of three calls per unresponsive patient were attempted, typically one in the morning, one in the afternoon and one in the evening. It was important to do this to minimise the influence of work status on ability to consider participation in the study. If a person could not be contacted (e.g. a correct number was unavailable or they did not answer), they were posted a letter asking them to contact the team if they were interested in participating. The sending of a letter was not in the original protocol; this was a substantial amendment and, with funder and governance approval, incorporated into protocol 1.2 (9 June 2016).

Randomisation

Computer-generated randomisation was conducted remotely by the Liverpool Clinical Trials Centre [Clinical Trials Unit (CTU) registration number 12]. Following consent and completion of the baseline measures, the research worker entered the participant's information into an online system and sent a request for randomisation to the CTU. This ensured that randomisation was performed independently of the trial's research and statistical teams.

Patient participants were randomised to either the SAFE plus TAU or TAU only arm. If they were taking part with an SO, the patient and SO were randomised as a dyad. The unit of randomisation was the individual patient. Patients were randomised to intervention or control at a ratio of 1 : 1 and randomisation used a web-based minimisation program with a built-in random element utilising stratification factors that were not made known to the researcher (DS) involved in data collection to minimise any potential for predicting allocation.

Like most trials using stratification,[162] we limited stratification to two factors. We selected factors based on evidence of their potential importance in influencing ED use and also pragmatic considerations. The factors chosen were recruitment site from which a patient participant was identified and whether or not the patient reported, at baseline, feeling stigmatised by epilepsy.

The reason for stratifying by recruitment site was that people who reside in more socially deprived areas are found to be more likely to use EDs[46,47] and because the catchment areas of the three ED recruitment sites were not completely equal in deprivation. The reason for stratifying by felt stigma was because, as reported in *Chapter 1*, Ridsdale *et al.*[27,31,32] found felt stigma to be a possible predictor of ED use and that it held a similarly sized relationship with subsequent ED use as mastery/confidence managing epilepsy.[27,128] It was not considered ideal to stratify by mastery/confidence in epilepsy because mastery/confidence in epilepsy is typically measured on a quasi-continuous rather than categorical scale and so stratifying patients would have required transformation of scores prior to randomisation by the research worker (DS), whom we sought to keep blind to stratification factors.

Blinding and protection from bias

This was a single-blind (outcome assessors blinded) pilot trial. All participants were aware of their treatment allocation. The trial statistician (SN), senior trial statistician (CTS) and the research worker (DS) responsible for consent, data collection and the conducting of outcome assessments were not. Participants were asked not to inform the research worker of their treatment allocation and were reminded of this at the start of each data collection point.

Allocation concealment was maintained by e-mail confirmations being automatically generated each time a participant randomisation was requested by the research worker and these being sent to relevant staff with or without details of the treatment allocation included, depending on their role in the study. The research worker submitting the request received only confirmation of successful randomisation, whereas an administrator was notified of persons randomisation to SAFE. The administrator liaised with patients (and their SOs) to arrange attendance at a SAFE course. Participants' usual care providers were informed of the patient's involvement in the trial but not of treatment allocation.

To evaluate how the blinding process worked, the research worker completed a 'research worker treatment guess' form after the follow-up assessment at 12 months or after withdrawal, and reported the circumstances of any unblinding.

People with epilepsy attending SAFE courses did so outside their routine clinic appointments and so we did not expect transfer of SAFE-related knowledge (and therefore contamination of the TAU arm) between those in the SAFE plus TAU and TAU only arms at a single site.

Intervention delivery

The SAFE intervention has been fully described in *Chapter 2*. Materials for the course included Microsoft PowerPoint (Microsoft Corporation, Redmond, WA, USA) presentation slides, videos illustrating seizure types, the recovery position and appropriate first aid. Patients took copies of the slides and additional information booklets (such as on risk management and emergency medication) away with them and could access and share a website of the course's content.

For the purposes of the pilot RCT, a single facilitator (Juliet Bransgrove; see *Acknowledgements*), recommended by the ES, was trained to deliver SAFE — She is a registered nurse with 30 years' experience (18 months as an epilepsy nurse) who delivered the ES's original course. Her training in the delivery of the revised intervention involved her familiarising herself with the trainer manual, delivering two practice courses with participants outside the trial and receiving feedback from the intervention development panel.

The SAFE courses were delivered in the education centre of a local teaching hospital, chosen because it was accessible and limited the distance participants needed to travel (i.e. it was near a major transport hub and centrally located), familiar to the patients and had access to emergency care services, if required.

To facilitate group interaction, chairs were arranged in a semicircle. A flip chart was set up for writing notes and discussion points. Workbooks, pens and name badges were ready for participants on arrival.

An administrator was present at each course to support its running. This included audio-recording the sessions and noting participant attendance. If a participant was present at the start and end of the course, it was considered that they had received the intervention in full. If a participant was unable to attend their scheduled course, the administrator attempted to contact them to identify the reason(s) and offer an alternative course date if appropriate and available.

All data on attendance and the communications between the administrator and participants to arrange attendance were inputted by them into a secure electronic database. These data were not accessible to the researcher responsible for participant recruitment and follow-up.

Data collection tools and follow-up visits

Primary

The proposed primary outcome measure for a definitive trial of SAFE would be subsequent ED use. This would require data on the number of ED visits each participant made over the 12 months following recruitment. In the pilot trial these data were sought from the NHS's Hospital Episode Statistics (HES) system. This system is theoretically able to identify, among other things, the number of attendances a patient has made at all EDs in England. It is primarily an administrative system, but, with explicit patient consent, governance approvals and payment of a fee, it is possible to apply to NHS Digital for this HES system to be interrogated for research purposes. For the pilot RCT a request was thus submitted for the HES system to be searched for ED attendances within specified time periods by the patient participants (using their unique NHS numbers). Because evidence was available at the time that indicated that for $\approx$ 30% of ED visits no diagnosis is recorded,[161] we requested data on the total number of ED visits made for any reason by individual patient participants during specified periods. Information on the number of visits each person had made over the 12 months prior to randomisation was also sought for the purpose of adjustment within the analyses and to allow comparison of self-reported ED use with routine data.

Secondary

The secondary outcome measures (*Table 4*) were based on participant self-report and collected using clinical research forms (CRFs). Baseline (T0) and follow-up at 12 months (T3) measures were completed during face-to-face sessions with a research worker (DS). During these appointments (and in line with completion guidelines), patient or SO participants completed their questionnaire by themselves, with the research worker offering assistance only if requested. An abbreviated questionnaire assessment occurred at follow-up at 6 months (T2); participants were posted a set of questionnaires for completion and instructed to return them in a pre-paid envelope.

TABLE 4 Self-reported outcome measures by assessment and participant type

Outcome	Participants	Measure and derivation of outcome	Baseline (T0)	3 months (T1)	6 months (T2)	12 months (T3)
ED visits	PWE	At baseline (T0): *How many times have you used the following hospital and day care services over the past 12 months for epilepsy? Casualty/accident and emergency department* At 6 months (T2): *You last saw our researcher for a face-to-face appointment about 6 months ago. Since then, have you visited a hospital accident and emergency (casualty) department for epilepsy? (No, not at all or yes)* *If Yes, how many times in total have you visited since your last face-to-face appointment with us?* At 12 months (T3): *During the past 12 months have you visited a hospital accident and emergency (casualty) department for epilepsy? (No or Yes)* *If yes, how many times in total have you visited during this time?*	✓	–	✓	✓
Fear of seizures	PWE; SOs	Epilepsy Knowledge and Management Questionnaire – fears subscale (five items)[163] Total fear score was calculated as the sum of the scores on the scale's five items, ranging from 5 to 30. Higher scores correspond to greater levels of fear	✓	–	–	✓
Knowledge of what to do when faced with a seizure	PWE; SOs	Items from Thinking About Epilepsy questionnaire (13 questions)[164] Knowledge score was calculated as the number of questions answered correctly (out of a total of 13). Only correctly answered questions were recorded. No down-weighting was applied for incorrectly answered questions or questions not answered	✓	–	–	✓
Confidence managing seizures/epilepsy	PWE; SOs	PWE: Wagner Mastery Scale (six items)[61] Total score was calculated as the sum of the scores on the scale's six items (with reverse weighting for two of the items), ranging from 6 to 24. Higher scores correspond to higher levels of mastery	✓	–	✓	✓

continued

TABLE 4 Self-reported outcome measures by assessment and participant type (*continued*)

Outcome	Participants	Measure and derivation of outcome	Baseline (T0)	3 months (T1)	6 months (T2)	12 months (T3)
		SO: Parental Response to Child Illness Scale – condition management subscale (six items)[165] Total score was calculated as the average of the scores, ranging from 1 to 5. A higher score corresponds to a higher level of confidence				
Quality of life	PWE	QOLIE-31-P (31 items)[166] Total QOLIE-31-P score was calculated, ranging from 0 to 100. Higher scores correspond to a better quality of life	✓	–	✓	✓
Distress	PWE; SOs	[a]HADS (14 items)[167,168] Total anxiety score and total depression scores were calculated, ranging from 0 to 21. Higher scores correspond to higher levels of anxiety or depression, respectively. Anxiety and depression categories were defined based on the total anxiety or depression score as: • 0–7 – 'normal range' • 8–10 – 'suggestive of anxiety/depression' • 11–21 – 'probable anxiety/depression'	✓	–	–	✓
Seizure control	PWE	At baseline (T0): Thapar's seizure frequency scale[169] for the prior 12 months At 6 months (T2) and 12 months (T3): patients were asked for number of seizures (any type) since the last assessment and dates of the first and most recent. (To assist, patients were offered a seizure diary at baseline)	✓	–	✓	✓
Felt stigma	PWE; SOs	Stigma Scale of Epilepsy (9 items)[62] Total stigma score calculated as sum scores on three items of scale, ranging from 0 to 9. Higher scores correspond to higher levels of stigma. Stigma categories were defined as: • 0 – 'no stigma' • 1–6 – 'mildly to moderately stigmatised' • 7–9 – 'highly stigmatised'	✓	–	–	✓

TABLE 4 Self-reported outcome measures by assessment and participant type (*continued*)

Outcome	Participants	Measure and derivation of outcome	Baseline (T0)	3 months (T1)	6 months (T2)	12 months (T3)
Burden	SOs	Zarit caregiver burden[170] Total burden score calculated as sum of scores on the measure's 22 items, ranging from 0 to 88. Higher scores correspond to a greater burden. Burden categories were defined as: • 0–20 – 'little or no burden' • 21–40 – 'mild to moderate burden' • 41–60 – 'moderate to severe burden' • 61–88 – 'severe burden'	✓	–	✓	✓
Health economics	PWE	Client Service Receipt[171] and EQ-5D (13 items)[172]	✓	–	–	✓
Feedback on trial participation	PWE; SOs	Adapted from Magpie Trial (three items)[173] 1. *If time suddenly went backward, and you had to do it all over again, would you agree to participate in the Seizure First Aid Training trial?* 2. *Please tell us if there was anything about the Seizure First Aid Training Trial that you think could have been done better* 3. *Please tell us if there was anything about the Seizure First Aid Training Trial, or your experience of joining the trial, that you think was particularly good*	–	–	–	✓

EQ-5D, EuroQol-5 Dimensions; HADS, Hospital Anxiety and Depression Scale; QOLIE-31-P, Quality of Life in Epilepsy Scale-31-P.
a This measure was used with permission from GL Assessment Ltd (London, UK), granted 17 July 2015.

The use of routine outcome data in clinical trials is advocated by the NIHR. However, limited evidence on its utility exists (see, for example, Powell *et al.*[174]). The pilot provided an opportunity to explore the ease and costs of obtaining routine data, the time it took for routine data to be secured, the proportion of participants the data covered and, finally, how routinely collected administrative data on ED use compared with self-reported data.

Adverse events

As part of the trial, patient participants did not receive additional medical reviews. Therefore, the experience of adverse events was monitored by asking them to complete a standardised checklist as part of the CRF at 3 months (T1; by telephone), 6 months (T2; by telephone) and 12 months (T3; during a face-to-face appointment) post randomisation.

Defining the outcomes

Primary

The proposed primary outcome measure for a future definitive trial is the number of epilepsy-related ED visits patient participants made over the 12 months following randomisation.

Secondary

There is currently no core outcome set for epilepsy.[175] A number of measures described in *Table 4* were used to assess secondary outcomes considered to be potentially important to capture in a definitive trial.

Participants in the pilot trial were assessed using the secondary outcome measures to permit the sample to be fully described according to them at baseline in order to accurately model potential burden of participation in a definitive trial and to allow us to describe completeness of data on these measures. A full description on these measures is provided in *Appendix 8*.

Adverse events

What constituted a serious adverse event (SAE) and how judgements regarding their relatedness to participation were made are described in *Appendix 9*.

Sample size

Because this was a pilot RCT, a formal power calculation to permit it to be able to detect a clinically meaningful difference in the primary outcome between SAFE plus TAU and TAU arms was not appropriate. Rather, the aim was to provide robust estimates of the likely rates of recruitment, consent and follow-up and to yield estimates of the ED event rate and dispersion parameter to accurately inform power calculations for a future definitive trial. To be able to do this, it was considered that 40 patients in each treatment arm would provide these estimates with adequate precision.

We estimated that $\geq$ 20% of those who have visited an ED on two or more occasions in the prior 12 months would agree to participate. It was anticipated that $\approx$ 400 eligible PWE would have visited the three ED recruitment sites over the 12 months preceding our recruitment phase. This was informed by NHS Digital data on the number of attendances at the sites in 2012/13[176] and audit data that show that $\approx$ 1% of all ED visits are for epilepsy and $\approx$ 80% are by those with an established diagnosis.[23,177] We also factored in evidence on the proportion of ED visits within 1 year that had been made by the same individual[20] and estimated, using data from Ridsdale *et al.*,[178] the number of PWE that would satisfy the inclusion/exclusion criteria.

With a sample size of 80, a participation rate of 20% could be estimated to within a 95% confidence interval (CI) of $\pm$ 4% and a drop-out rate of 25% to within a 95% CI of $\pm$ 10%. Assuming that data on the proposed primary outcome measure of ED visits at 12 months were not available for 25% of patients, outcome data from 60 patients would still allow robust estimation of the ED rate and dispersion parameter. We considered that one full-time researcher would be able to recruit the required sample within 8 months.

Completion of follow-ups

A number of evidence-based strategies were used to maximise retention of participants in the trial.[179] This included patient and SO participants receiving a £10 shopping voucher after each follow-up assessment that they completed and delayed access to SAFE for the TAU arm.

Unless a participant formally withdrew consent to participate in the trial, HES data on them were requested and up to three attempts were made to contact patients or SO participants each time a follow-up assessment was due. The research worker also contacted participants by telephone approximately 2 weeks after the 6-month questionnaires were posted.

When a patient participant did not complete a follow-up assessment, an attempt to monitor SAEs was made by sending their GP a letter asking them to inform us if the patient was no longer alive and the circumstances of death.

Data management

With the exception of the routine outcome data on ED use from NHS Digital, all data were collected on paper-based CRFs by the research worker. The CRFs were kept in locked filing cabinets in a central research office with restricted access at the University of Liverpool. The paper CRFs were sent to the CTU for entry into MACRO 4.0 (Elsevier, Amsterdam, the Netherlands) by a data manager. At the point of data entry, queries were raised. Participant contact information was kept on a secure central network server with access granted to study staff only.

Data analysis

All statistical analyses were performed with SAS® statistical software (version 9.4) (SAS Institute Inc., Cary, NC, USA) (by SN; overseen by CTS). A full statistical analysis plan was developed and approved prior to conducting the final analysis.

Rates of eligibility, consent, recruitment, retention and unblinding

Derivation and statistical analysis

The eligibility rate is defined as the percentage of patients screened that satisfy eligibility criteria (see *Chapter 3*). The consent rate is defined as the percentage of eligible patients who provided informed, written consent for randomisation. The recruitment rate is defined as the number of participants recruited per calendar month.

Eligibility and consent rates are presented as percentages with 95% CIs. Recruitment rates are presented as the actual number of participants recruited per calendar month presented alongside the expected number of participants recruited per calendar month on recruitment graphs.

The age, sex and social deprivation profiles (available from ED records) of eligible individuals who did and did not consent to take part in the trial are presented side by side in table columns for visual comparison to evaluate representativeness of the trial sample.

Retention rate is defined as the percentage of randomised patient and SO participants completing 3, 6 and 12 months of the study without withdrawing (i.e. without formally withdrawing from any further data collection). Reasons for withdrawal, where known, are presented.

The completion rate of study assessment tools (i.e. the percentage of patient and SO participants completing each measure outlined in *Table 4*) is presented as an indicator of retention and participation in the trial.

The unblinding rate is defined as the proportion of correct treatment allocation guesses made by the research worker at the end of the trial (12 months) or at withdrawal of the participant from the trial. The unblinding rate is presented with 95% CIs. A Cohen's kappa statistic for agreement (i.e. the correct guess of allocation) and 95% CIs are also presented.

Demographic and baseline characteristics

Baseline characteristics are presented for PWE overall and by treatment arm with comparisons presented for a subset of characteristics for those individuals identified as eligible and invited to participate in the trial who did not agree to participate in the trial.

Relevant baseline characteristics are presented descriptively for SO participants.

Categorical data are summarised by numbers and percentages. Continuous data are summarised by mean, median, standard deviation (SD) and range (minimum and maximum values). Tests of statistical significance are not undertaken for baseline characteristics; rather, the potential clinical importance of any imbalance is noted.

Primary outcome: epilepsy-related emergency department visits

Derivation of outcome

The proposed primary outcome of a future trial is defined as the number of epilepsy-related ED visits made by patient participants over the 12 months following randomisation measured by HES data. As a secondary outcome, the number of self-reported epilepsy-related ED visits made by patient participants over the 12 months following randomisation is also presented.

Statistical analysis

Epilepsy-related ED visits are presented at baseline (T0) and at 12 months (T3), and the number of ED visits made by the end of the 12-month period compared with the number of ED visits made in the 12 months prior to baseline is also presented. Results are presented for all patient participants and by treatment arm as mean and SDs, in addition to the median, the minimum and the maximum number of epilepsy-related ED visits. Completeness of data for self-reported epilepsy-related ED visits is presented and no imputation of missing data was performed.

The difference between the SAFE plus TAU arm and TAU only arm is compared at 12 months with and without adjustment for baseline ED visits via negative binomial regression (NBR) models for count data. Overdispersion (i.e. variance larger than the mean) and an excess number of zeros for individuals who did not visit an ED in the last 12 months was anticipated; therefore, zero-inflated NBR models were also applied. The preferred model (negative binomial or zero-inflated negative binomial) was determined by Vuong's test.[180]

Between-arm differences are presented as rate ratios with 95% CIs and statistically tested according to a 5% level of significance. In addition, as per guidance for pilot trials,[181] 90% and 80% CIs are also presented to aid interpretation of between-arm differences.

Epilepsy-related ED visits, measured by HES data, were compared with self-reported epilepsy-related ED visits and Bland–Altman plots and limits of agreement statistics[182] were calculated to determine the agreement of the two measurement methods. A Bland–Altman plot shows the mean number of ED visits in self-reported and HES data for each patient participant (x-axis) and the difference in the number of ED visits in self-reported and HES data for each patient participant (y-axis). Bland–Altman limits of agreement (mean $\pm$ 2 SDs) of the difference in the number of ED visits are also shown on the plot. These limits can be interpreted as the level of agreement that is 'acceptable' between the two measurements of recording ED visits.

Estimation of sample size of a future definitive trial

The average annual rate of ED visits in the SAFE plus TAU and TAU only arms and the likely dispersion parameter estimated from the preferred NBR model are used to estimate the sample size of a future definitive trial according to the methods outlined by Keene *et al.*[183] for a negative binomial regression.

The number of patient participants required per arm in a definitive trial to detect the size of the effect shown in the pilot study is:

$$n = \left\{\frac{z_{1-\beta} + z_{1-\alpha/2}}{\log(\mu_1/\mu_2)}\right\}^2 \times \left\{\frac{\mu_1 + \mu_2}{\mu_1\mu_2} + 2k\right\}, \quad (1)$$

where $Z_{1-\alpha/2}$ and $Z_{1-\beta}$ are critical values of the normal distribution for specific values of α and β (typically, $\alpha = 0.05$ for a 5% significance level and $\beta = 0.2$ or 0.1 for 80% or 90% power, respectively), μ_1 and μ_2 are the estimated ED rates from the two treatment arms and k is the negative binomial shape parameter from the associated gamma distribution, which explicitly represents variability between subjects.

Secondary outcome measures

Derivation of outcomes

Details of the secondary outcome measures are described in *Table 4*.

Total scores for Quality of Life in Epilepsy Scale-31 item-Patient-weighted (QOLIE-31-P) (PWE participants only), burden (SO participants only), confidence in managing seizures/epilepsy (SO participants only), mastery (PWE participants only) and fear of seizures (PWE and SO participants) are presented at baseline (T0), 6 months (T2) and 12 months (T3). The changes in total scores at 6 months (T2) and 12 months (T3) from baseline (T0) are presented. Burden categories ('little or no burden', 'mild to moderate burden', 'moderate to severe burden' and 'severe burden') are presented.

Total scores for stigma (PWE participants only) and distress (anxiety and depression scores; PWE and SO participants) are presented at baseline (T0) and at 12 months (T3). The changes in total scores at 12 months (T3) from baseline (T0) are also presented and stigma categories ('no stigma', 'mildly to moderately stigmatised' and 'highly stigmatised') and anxiety and depression categories ('normal range', 'suggestive of anxiety/depression' and 'probable anxiety/depression') are presented.

The 'knowledge of what to do where faced with a seizure' score is presented as the number of questions answered correctly (out of 13) at baseline (T0) and at 12 months (T3), in addition to the change in knowledge score at 12 months (T3) from baseline (T0).

Self-reported seizure frequency is presented at baseline (T0), at 6 months (T2) and at 12 months (T3) according to Thapar's seizure frequency scale.[169] The total numbers of seizures between baseline (T0) and 6 months (T2) and between baseline (T0) and 12 months (T3) are also presented.

Statistical analysis

Total scores and the change from baseline scores of all measures, plus the total number of seizures, are presented as mean and SD in addition to the median, the minimum and the maximum scores for each scale. Burden, stigma, anxiety and depression categories are also presented as the number and percentage of participants in each category. Results are presented for all participants and by treatment arm and separately for PWE and SO participants where applicable.

Completeness of data for all self-reported scales is presented. Individual missing values in given scales of the QOLIE-31-P[184] and the Hospital Anxiety and Depression Scale (HADS) scale were imputed according to recommended rules.[185] No imputation was performed for other scales. Total scores are presented separately for all individuals (including those with missing data) and for individuals with complete data for the scale.

Visual comparison of differences between treatment arms only are made for secondary outcome measures; no formal statistical testing is performed.

Chapter 4 Part B: pilot RCT – recruitment, retention, intervention delivery and participant baseline characteristics

Introduction

This chapter presents findings from the pilot trial relating to participant recruitment, retention and attendance at SAFE intervention sessions.

Participant flow through study

Search period

The stage 1 searches were originally set up to identify PWE who had made an ED visit between 1 January 2015 and 31 December 2015. However, recruitment proved more challenging than anticipated and, with funder and governance approval, the period in which people could be identified as having attended the EDs was extended by 7 months to 31 July 2016 (minor amendment, incorporated into protocol version 1.2 on 9 July 2016). A total of 417,381 attendances for any reason were recorded at the EDs between 1 January 2015 and 31 July 2016.

Eligibility

The stage 1 searches indicated that 6359 (1.5%) of the ED attendances were attributable to epilepsy or a suspected epileptic seizure. These visits had been made by 4016 individuals. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram is presented (*Figure 3*). Following stage 2 review of the triage card associated with these visits, 1220 individuals were considered to have visited for established epilepsy, with 555 of them being considered eligible for participation in the trial and sent an invitation.

Having received the letter, no patient opted out, but 122 patients did send notification that they were ineligible (*Tables 5–7*). For nine patients the postal address was incorrect or the letter was not sent, in error. The remaining 424 patients were telephoned to determine their interest in the study and verify eligibility (stage 3). Based on these figures, the eligibility rate (424 eligible participants out of 4016 unique individuals screened) was 10.6% (95% CI 9.6% to 11.5%).

It took the local principal investigator at each site $\approx$ 3 full days to complete the stage 2 screening.

Recruitment rates and speed of recruitment

The process of enrolment (i.e. participant consent and baseline assessment, as opposed to the period within which the participants' ED visits must have occurred) began in May 2016 and concluded at the end of December 2016. Among the 424 patients telephoned, 53 agreed to participate and provided informed consent, thus giving a consent rate of 12.5% (95% CI 9.3% to 15.6%). The reasons participants offered for not taking part are provided in *Table 8*.

Regarding consent, successful telephone contact could be made with only 203 out of the 424 (47.9%) eligible patients. When restricted to those who could be contacted, the consent rate is 26.1% (95% CI 20.0% to 32.2%).

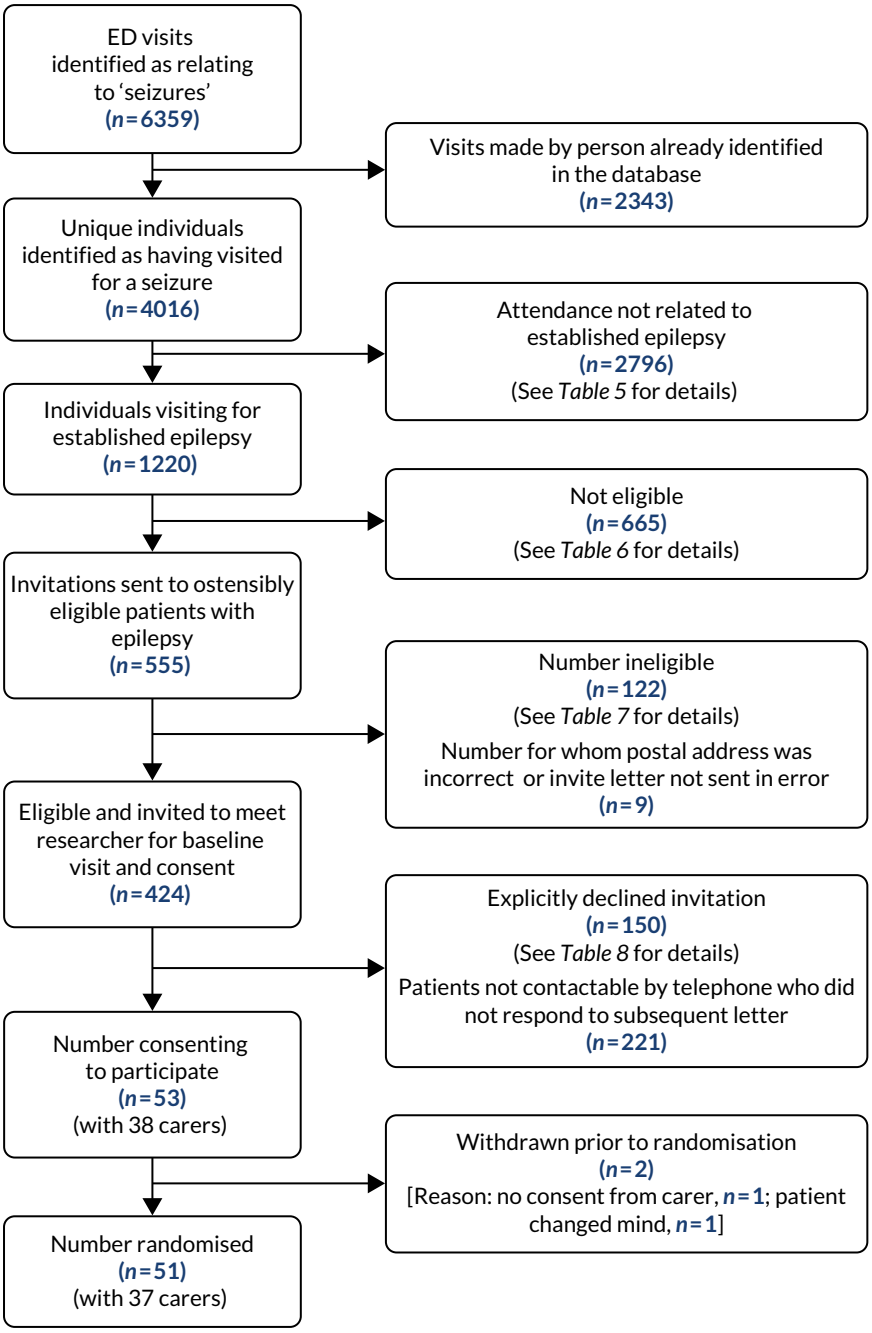

FIGURE 3 The CONSORT flow diagram of eligibility screening for the trial.

TABLE 5 Attendance at ED not related to epilepsy

Reason	Number of participants			
	Site 1	Site 2	Site 3	Total
No confirmed diagnosis of epilepsy/not attending because of epilepsy	737	483	715	1935
Acute symptomatic seizures related to neurological illness or substance abuse	238	240	191	669
Psychogenic non-epileptic seizures	19	55	29	103
Medical record missing	54	5	27	86
Ineligible, no reason given[a]	2	1	0	3
Total	1050	784	962	2796

a Lack of reason due to patients returning participation slips without stating actual reason for ineligibility.

TABLE 6 Other reasons for non-eligibility (individuals visiting for established epilepsy)

Reason	Number of participants			
	Site 1	Site 2	Site 3	Total
Postcode outside catchment area	148	94	60	302
Learning disability likely to impede individuals' capacity to provided signed, informed consent	45	51	52	148
Inability to converse in English and provide signed informed consent	10	24	46	80
Life-threatening medical illness	35	26	10	71
Severe psychiatric disorder	11	3	18	32
No fixed abode	10	6	13	29
Participating in another trial	3	0	0	3
Total	262	204	199	665

TABLE 7 Reasons for non-eligibility (ostensibly eligible individuals)

Reason	Number of participants			
	Site 1	Site 2	Site 3	Total
Has not visited an ED for epilepsy on two or more occasions in previous 12 months (self-reported)	9	15	24	48
Not able to provide informed consent, participate in SAFE course if randomised or to independently complete questionnaires in English	9	7	7	23
Ineligible, no reason given[a]	4	7	4	15
No established diagnosis of epilepsy (< 1 year)	3	2	5	10
Moved out of area; postcode no longer within 25-mile catchment area	4	1	3	8
Actual or suspected psychogenic non-epileptic seizures alone or in combination with epilepsy	2	1	4	7
Severe current psychiatric disorders or life-threatening medical illness	1	5	1	7
Not currently being prescribed antiepileptic drug	1	0	1	2
Acute symptomatic seizures related to acute neurological illness or substance misuse	0	1	0	1
Participating in another trial	1	0	0	1
Total	34	39	49	122

a Lack of reason due to patients returning participation slips without stating actual reason for ineligibility.

TABLE 8 Reasons for declining participation (eligible individuals)

Reason	Number of participants			
	Site 1	Site 2	Site 3	Total
Not interested	30	11	23	64
Too busy	11	12	11	34
No reason given	9	10	8	27
Too ill	5	5	9	19
Too well	3	1	2	6
Total	58	39	53	150

The process of enrolment lasted 226 days (equivalent to 7.43 months), with an average randomisation rate of 6.9 patients per month (ranging from 4 to 11 patients per month). Actual rates and expected rates of recruitment each month are presented in *Appendix 10*. Because the target sample size of 80 patients was not reached, the speed of recruitment could not be calculated.

Randomisation

Among the 53 consenting patients, 51 were randomised (along with 37 SO participants with whom they took part). The first was randomised on 19 May 2016 and the last on 31 December 2016. Two patient participants were not randomised because they withdrew prior to randomisation.

Among the 51 patient participants randomised, 26 (with 18 SOs) were allocated to SAFE plus TAU and 25 (with 19 SOs) to TAU only. Participant flow through the SAFE trial is outlined in *Figure 4*.

Receipt of intervention

Seven SAFE intervention courses were run for the SAFE plus TAU arm between June 2016 and February 2017. No seizures were recorded as having occurred during the courses and there were no instances of participants in the TAU arm attending a SAFE session by mistake.

We anticipated that SAFE would be delivered to groups of 8–10 people in the pilot trial. In practice, the average group size was 5, with 20 (76.9%) out of the 26 patient participants and 13 (72.2%) out of the 18 SOs randomised to the intervention attending a course. No patients or SOs completed only part of a course.

A total of 33 course bookings were made for the 26 patient participants randomised to SAFE. Most ($n = 18$, 90%) of the 20 patient participants randomised to SAFE who actually attended a course attended the first course that they were booked on. The minority of patients who did not ultimately attend a course were associated with substantial administrative activity. Specifically, six patient participants who did not attend a course received, between them, 45 telephone calls from the study administrator and booked onto 11 course slots. This contrasts with the 34 telephone calls in total that were made to the 20 patient participants who attended a course. Reasons for non-attendance included poor health on the patients' behalf and work commitments on behalf of the SO.

Withdrawals and completion of follow-ups

Formal withdrawals from trial

Among the 51 randomised patient participants, only three (5.9%) withdrew consent to participate and for routine data to be collected on them over the course of their 12 months in the trial; two withdrew from the TAU condition and one from the SAFE arm. This meant that consent remained in place for securing routine outcome ED data for 48 (94.1%) patient participants. The reasons for participant withdrawal are described in *Appendix 11*. No withdrawals were initiated on the patient's behalf by a health-care provider or a member of the research team. Among the 37 randomised SO participants, five (13.5%) withdrew.

Participation in questionnaire-based follow-up assessments

A total of 37 (72.5%) of the patient participants and 21 (56.8%) SOs attended their scheduled post-randomisation primary outcome assessment at 12 months (T3). The 37 patient participants attended their post-randomisation follow-up visit at 12 months at a median of 286 days (range 252–365 days) post randomisation. Appointments often took place before 12 months because slower recruitment meant that time for follow-up within the life of the project was reduced.

With respect to the interim questionnaire assessments, 43 (84.3%) patients returned the 3-month (T1) follow-up questionnaire and 39 (76.5%) patients and 26 (70.3%) SOs returned their 6-month (T2) follow-up questionnaire.

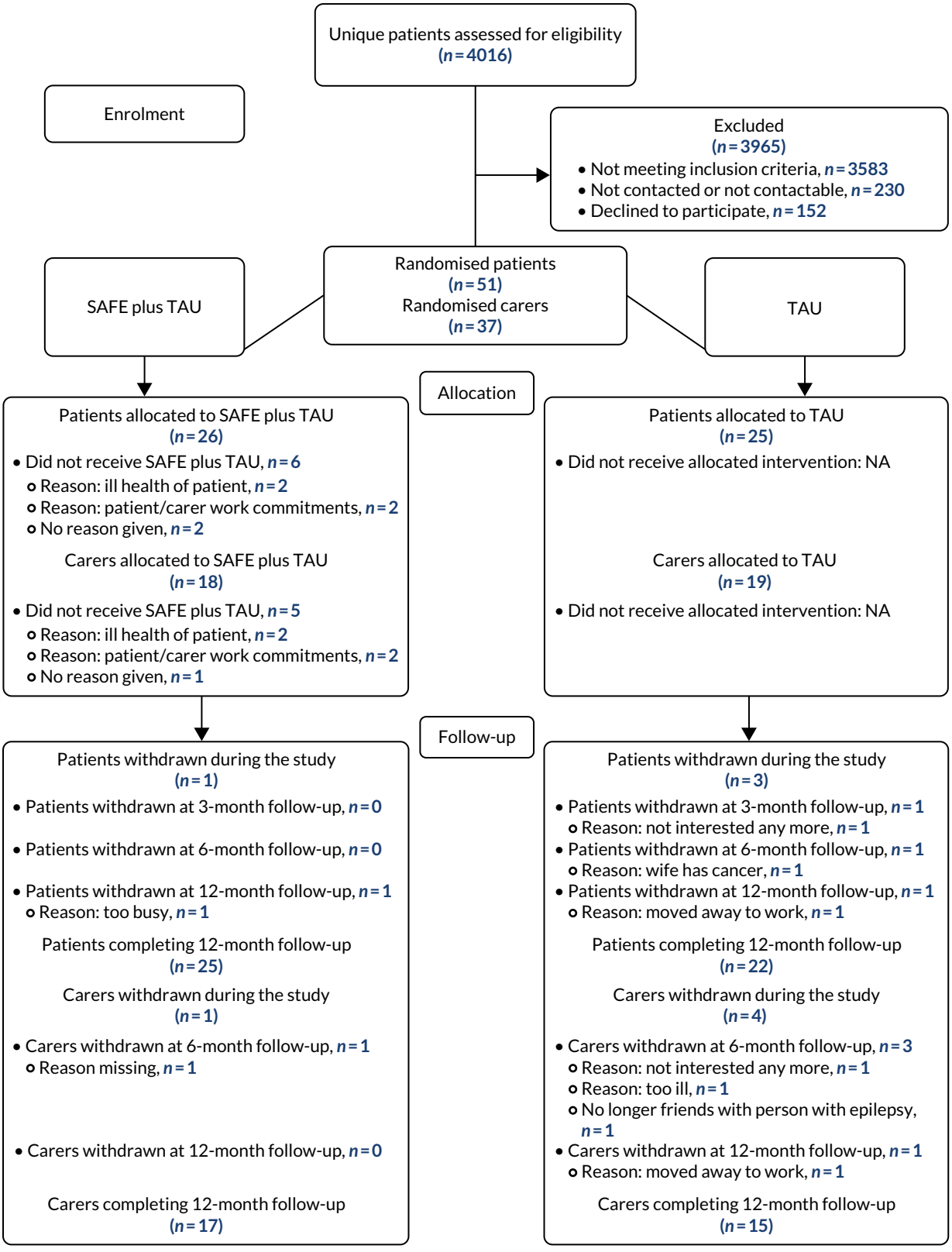

FIGURE 4 The CONSORT flow diagram for the SAFE trial. NA, not applicable.

Securing outcome data and their completeness

Primary outcome: emergency department data from Hospital Episode Statistics system

Completeness of data

Hospital Episode Statistics data on ED use were secured by the research team from NHS Digital for each of the 48 (94.1%) randomised patient participants for whom consent to participate and secure ED outcome data on them remained.

Process of securing the data

After delays in being granted permission to access NHS Digital's application form, the research team submitted the application for the data on 16 February 2018. To minimise cost, a single application, rather than one relating to the baseline period and one for follow-up, was submitted. The data were ultimately received by the research team on 31 October 2018 at a direct cost of £6960.00 [inclusive of value-added tax (VAT)].

Prior to starting the trial and submitting the application, the research team communicated with NHS Digital and ensured that the participant information sheet and consent form were consistent with its requirements. Despite this, it took 7 months for the application to be reviewed and approved by NHS Digital and an additional 1.5 months for the data file to be produced and transferred.

During these periods, substantial effort was required by the research team to respond to queries raised by NHS Digital and to request progress updates once responses had been submitted. A log of all correspondence was kept by the research team. The team typically responded to queries raised by NHS Digital within 1 day; key milestones are outlined in *Appendix 12*. In one instance, the research team needed to successfully appeal – 5 months into the application process – against a decision by NHS Digital to reject it because of, among other things, apprehensions regarding the project's scientific merit. The team was notified it was being rejected because of 'concerns [over . . .] whether this pilot would yield findings that were statistically valuable to achieve the stated aims given the small numbers involved'.

Secondary outcome data

The extent to which the secondary outcome measures were fully completed by the patient participants who participated in the follow-up assessments varied by assessment point, by measure and by participant type (*Tables 9* and *10*). Self-reported ED use at 12 months post randomisation (T3) by patient participants was the secondary means by which ED use was captured and so, arguably, the most important of the secondary outcome measures. Self-reported ED use data at 12 months (T3) were available for 34 (66.7%) out of the 51 randomised patient participants.

Baseline characteristics

Patient participants

Demographics

The mean age of the 51 randomised patient participants was 39.9 years (SD 15.6 years, range 16–71 years); 29 (56.9%) were female and 94.1% identified themselves as being of 'white' ethnicity (*Table 11*).
The Index of Multiple Deprivation (IMD) (URL: www.gov.uk/government/statistics/english-indices-of-deprivation-2015; accessed 27 August 2019), measuring levels of deprivation according to participants' home postcode, indicated that most (74.4%) patient participants lived in areas of high deprivation; 49% ($n = 25$) lived in areas in the top 10% most socially deprived in the country. Most (53%) patient participants had attained a basic level of formal education only [i.e. Ordinary levels (O levels)/General Certificate of Secondary Educations (GCSEs)/Level 1 or 2 National Vocational Qualification (NVQ)].

TABLE 9 Number of patient participants fully completing study assessment tools at each time point

Study assessment tool	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Baseline (T0)	***(N = 26)***	***(N = 25)***	***(N = 51)***
ED self-report	24 (92.3)	21 (84.0)	45 (88.2)
Thapar's seizure frequency scale:[169] seizure control	26 (100.0)	25 (100.0)	51 (100.0)
QOLIE-31-P[184]	23 (88.5)	16 (64.0)	39 (76.5)
[a]HADS[167,168]	23 (88.5)	24 (96.0)	47 (92.2)
Stigma Scale of Epilepsy[62]	24 (92.3)	24 (96.0)	48 (94.1)
[b]Client Service Receipt Inventory[171]	19 (73.1)	17 (68.0)	36 (70.6)
EQ-5D[172]	21 (80.8)	25 (100.0)	46 (90.2)
Wagner 6-item Mastery Scale[61]	26 (100.0)	21 (84.0)	47 (92.2)
Epilepsy Knowledge and Management questionnaire:[163] fear of seizures subscale	16 (61.5)	9 (36.0)	25 (49.2)
6 months (T2)	***(N = 26)***	***(N = 23)[c]***	***(N = 49)[c]***
QOLIE-31-P[184]	16 (61.5)	12 (52.2)	28 (57.1)
Wagner 6-item Mastery Scale[61]	21 (80.8)	15 (65.2)	36 (73.5)
Thapar's seizure frequency scale:[169] seizure control	16 (61.5)	15 (65.2)	28 (57.1)
12 months (T3)	***(N = 25)[d]***	***(N = 22)[d]***	***(N = 47)[d]***
ED self-report	17 (68.0)	17 (77.3)	34 (72.3)
Thapar's seizure frequency scale:[169] seizure control	20 (80.0)	14 (60.9)	34 (72.3)
QOLIE-31-P[184]	10 (40.0)	8 (36.4)	18 (38.3)
[a]HADS[167,168]	18 (72.0)	17 (77.3)	35 (74.4)
Stigma Scale of Epilepsy[62]	18 (72.0)	17 (77.3)	35 (74.4)
[b]Client Service Receipt Inventory[171]	13 (52.0)	10 (45.5)	23 (48.9)
EQ-5D[172]	18 (72.0)	17 (77.3)	35 (74.4)
Wagner 6-item Mastery Scale[61]	18 (72.0)	16 (72.7)	34 (72.3)
Epilepsy Knowledge and Management questionnaire:[163] fear of seizures subscale	8 (32.0)	5 (22.7)	13 (27.7)
Feedback on participation	17 (68.0)	15 (68.2)	32 (68.1)

EQ-5D, EuroQol-5 Dimensions.
a Completeness of the whole HADS scale (both anxiety and depression subscales).
b Only six mandatory questions counted. Conditional questions (e.g. 'if yes, then') were not counted towards total completion.
c Two patient participants from the TAU arm had withdrawn by the 6-month visit.
d Four patient participants (three from the TAU arm and one from the SAFE plus TAU arm) had withdrawn by the 12-month visit.
Although some participants did not fully complete all items in a questionnaire, this does not mean that their data would automatically need to be excluded from analysis of a change in that domain because for some measures test developers permit imputation when the number of missing items is small and follows a specific pattern. Information on the number of items completed for the specific assessment tools is presented in *Appendix 13*.

TABLE 10 Number of SO participants fully completing study assessment tools at each time point

Study assessment tool	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Baseline (T0)	***(N = 18)***	***(N = 19)***	***(N = 37)***
Zarit caregiver burden[170]	17 (94.4)	17 (89.5)	34 (91.9)
[a]HADS[167,168]	17 (94.4)	18 (94.7)	35 (94.6)
Parent Response to Child Illness scale[186]	18 (100.0)	19 (100.0)	37 (100.0)
Epilepsy Knowledge and Management questionnaire:[163] fear of seizures subscale	6 (33.3)	4 (21.1)	10 (27.0)
6 months (T2)	***(N = 17)***[b]	***(N = 16)***[b]	***(N = 33)***[b]
Zarit caregiver burden[170]	15 (88.2)	8 (50.0)	23 (69.7)
Parent Response to Child Illness scale[186]	16 (94.1)	9 (56.3)	25 (75.8)
12 months (T3)	***(N = 17)***[c]	***(N = 15)***[c]	***(N = 32)***[c]
Zarit caregiver burden[170]	11 (64.7)	10 (66.7)	21 (65.6)
[a]HADS[167,168]	11 (64.7)	10 (66.7)	21 (65.6)
Parent Response to Child Illness scale[186]	11 (64.7)	10 (66.7)	21 (65.6)
Epilepsy Knowledge and Management questionnaire:[163] fear of seizures subscale	6 (35.3)	2 (13.3)	8 (25.0)
Feedback on participation	11 (64.7)	9 (60.0)	20 (62.5)

a Completeness of the whole HADS scale (both anxiety and depression subscales).
b Four SO participants (one in the SAFE plus TAU arm and three in the TAU arm) had withdrawn by the 6-month visit.
c Five SO participants (one in the SAFE plus TAU arm and four in the TAU arm) had withdrawn by the 3-month visit.
Although some participants did not fully complete all items in a questionnaire, this does not mean that their data would automatically need to be excluded from analysis of a change in that domain because for some measures test developers permit imputation when the number of missing items is small and follows a specific pattern. Information on the number of items completed for the specific assessment tools is presented in *Appendix 13*.

TABLE 11 Demographic characteristics of patient participants

Demographic characteristic	Treatment arm		Total
	SAFE plus TAU	TAU	
Sex*, n *(%)	***(N = 26)***	***(N = 25)***	***(N = 51)***
Male	10 (38.5)	12 (48.0)	22 (43.1)
Female	16 (61.5)	13 (52.0)	29 (56.9)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Age (years) at presentation to the ED[a]	***(N = 26)***	***(N = 25)***	***(N = 51)***
Mean, years	39.2	40.7	39.9
SD, years	13.96	17.52	15.66
Minimum, years	18.9	16.5	16.4
Median, years	37.1	41.4	38.8
Maximum, years	69.9	71.3	71.3
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)

TABLE 11 Demographic characteristics of patient participants (*continued*)

Demographic characteristic	Treatment arm		Total
	SAFE plus TAU	TAU	
IMD[b]	***(N = 26)***	***(N = 25)***	***(N = 51)***
Decile 1			
n (%)	11 (42.3)	14 (56.0)	25 (49.0)
Minimum rank	44	48	44
Median rank	574.0	1231.5	673.0
Maximum rank	3202	2166	3202
Deciles 2 and 3			
n (%)	7 (26.9)	6 (24.0)	13 (25.4)
Minimum rank	4649	3989	3989
Median rank	6785	6665	6785
Maximum rank	8281	7816	8281
Deciles 4–6			
n (%)	2 (7.7)	4 (16.0)	6 (11.8)
Minimum rank	9881	11,480	9881
Median rank	12,836	11,924	11,924
Maximum rank	15,791	16,004	16,004
Deciles 7–10			
n (%)	5 (19.2)	1 (4.0)	6 (11.8)
Minimum rank	24,971	32,724	24,971
Median rank	27,642	32,724	28,876
Maximum rank	31,002	32,724	32,724
Decile missing[c]			
n (%)	1 (3.8)	0 (0.0)	1 (2.0)
Ethnicity,* n *(%)	***(N = 26)***	***(N = 25)***	***(N = 51)***
White	25 (96.2)	23 (92.0)	48 (94.1)
Asian/Asian British	0 (0.0)	0 (0.0)	0 (0.0)
Black/African/Caribbean/black British	1 (3.8)	1 (4.0)	2 (3.9)
Mixed/multiple	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	1 (4.0)	1 (2.0)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Other significant medical history,* n *(%)	***(N = 26)***	***(N = 25)***	***(N = 51)***
No, none	13 (50.0)	10 (40.0)	23 (45.1)
Yes, another medical condition(s)	10 (38.5)	13 (52.0)	23 (45.1)
Yes, a psychiatric condition	1 (3.8)	0 (0.0)	1 (2.0)
Yes, both medical and psychiatric conditions	2 (7.7)	2 (8.0)	4 (7.8)
Missing	0 (0.0)	0 (0.0)	0 (0.0)

continued

TABLE 11 Demographic characteristics of patient participants (*continued*)

Demographic characteristic	Treatment arm		Total
	SAFE plus TAU	TAU	
Education*, n *(%)	***(N = 26)***	***(N = 25)***	***(N = 51)***
O levels/GCSEs/Level 1 or 2 NVQ	13 (50.0)	14 (56.0)	27 (53.0)
A levels/Level 3 NVQ	5 (19.2)	3 (12.0)	8 (15.7)
University degree/graduate certificate or diploma	5 (19.2)	5 (20.0)	10 (19.6)
Postgraduate university degree (e.g. PGCE, MSc, MA, PhD)	2 (7.7)	0 (0.0)	2 (3.9)
Missing	1 (3.9)	3 (12.0)	4 (7.8)

A level, Advanced level; MA, Master of Arts; MSc, Master of Science; PGCE, Postgraduate Certificate in Education; PhD, Doctor of Philosophy.

a Four participants (7.8%) had missing ages recorded from CRF data; therefore, date of birth and date of presentation recorded in the bespoke screening database were used to calculate age at presentation to the ED.

b The IMD ranks every small area in England from 1 (most deprived area) to 32,844 (least deprived area). Decile and rank missing for one recruited participant because they resided in Wales.

Epilepsy characteristics

Patient participants had been diagnosed with epilepsy for a median of 21 years. Most participants (62.8%) reported having had ≥ 10 seizures in the previous year. Most participants (54.9%) reported having another health condition. The median time since their last seizure was 14 days. Most participants ($n = 38$; 74.5%) reported having seen a neurologist in the 12 months prior to their assessment (*Table 12*).

TABLE 12 Baseline disease characteristics and key health service use of patient participants

Disease characteristic	Treatment arm		Total
	SAFE plus TAU	TAU	
Time (years) since epilepsy diagnosis			
n (%)	26 (100.0)	25 (100.0)	51 (100.0)
Mean, years	19.9	22.6	21.2
SD, years	14.85	18.38	16.57
Minimum, years	1.8	1.7	1.7
Median, years	16.8	19.3	17.3
Maximum, years	53.9	64.9	64.9
Missing, *n (%)*	0 (0.0)	0 (0.0)	0 (0.0)
Time (days) since last epileptic seizure			
n (%)	23 (88.5)	22 (88.0)	45 (88.2)
Mean, days	53.6	40.1	47.0
SD, days	101.10	61.21	83.34
Minimum, days	1	0	0
Median, days	14.0	10.5	14.0
Maximum, days	340	235	340
Missing, *n (%)*	3 (11.5)	3 (12.0)	6 (11.8)

TABLE 12 Baseline disease characteristics and key health service use of patient participants (*continued*)

Disease characteristic	Treatment arm		Total
	SAFE plus TAU	TAU	
Number of epileptic seizures in the last 12 months			
n (%)	26 (100.0)	25 (100.0)	51 (100.0)
0	1 (3.8)	0 (0.0)	1 (2.0)
1	1 (3.8)	0 (0.0)	1 (2.0)
2	0 (0.0)	2 (8.0)	2 (3.9)
3	2 (7.7)	1 (4.0)	3 (5.9)
4	0 (0.0)	0 (0.0)	0 (0.0)
5	0 (0.0)	2 (8.0)	2 (3.9)
6	1 (3.8)	3 (12.0)	4 (7.8)
7	1 (3.8)	1 (4.0)	2 (3.9)
8	2 (7.7)	2 (8.0)	4 (7.8)
9	0 (0.0)	0 (0.0)	0 (0.0)
≥ 10	18 (69.2)	14 (56.0)	32 (62.8)
Missing, *n (%)*	0 (0.0)	0 (0.0)	0 (0.0)
HES health-care use in the last 12 months *ED attendance*			
n (%)	25 (96.2)	23 (92.0)	48 (94.1)
At least one attendance, *n (%)*[a]	23 (88.5)	18 (72.0)	41 (80.4)
Mean	2.1	3	2.5
SD	2.22	2.76	2.51
Minimum	0	1	0
Median	1	2	2
Maximum	10	12	12
Missing, *n (%)*	1 (3.8)	2 (8.0)	3 (5.9)
Self-reported health-care use in the last 12 months for epilepsy *ED attendance*			
n (%)	24 (92.2)	21 (84.0)	45 (88.2)
At least one attendance, *n (%)*[a]	23 (88.5)	18 (72.0)	41 (80.4)
Mean	4.3	9.8	6.7
SD	2.83	24.38	16.27
Minimum	1	1	1
Median	4	4	4
Maximum	12	107	107
Missing, *n (%)*	2 (7.8)	4 (16.0)	6 (11.8)
Neurology outpatient appointment			
n (%)	25 (96.2)	22 (88.0)	47 (92.1)
At least one attendance, *n (%)*[a]	21 (80.8)	16 (68.0)	38 (74.5)
Mean	2.6	3.1	2.8

continued

TABLE 12 Baseline disease characteristics and key health service use of patient participants (*continued*)

Disease characteristic	Treatment arm		Total
	SAFE plus TAU	TAU	
SD	1.78	2.26	2.00
Minimum	1	1	1
Median	2	2	2
Maximum	8	10	10
Missing, *n (%)*	1 (3.8)	3 (12.0)	4 (7.8)
Emergency ambulance called (whether or not the ambulance took the patient to the ED)			
n (%)	21 (80.8)	21 (84.0)	42 (82.4)
At least one attendance, *n (%)*[a]	18 (69.2)	18 (72.0)	36 (70.6)
Mean	3.2	4.1	3.6
SD	2.87	2.86	2.86
Minimum	1	1	1
Median	2	3	3
Maximum	12	12	12
Missing, *n (%)*	5 (19.2)	4 (16.0)	9 (17.7)
GP contact			
n (%)	23 (88.5)	23 (92.0)	46 (90.2)
At least one contact, *n (%)*[a]	16 (61.6)	13 (52.0)	29 (56.9)
Missing, *n (%)*	3 (11.5)	2 (8.0)	5 (9.8)
Number of contacts (if used)[a]			
Mean	3.7	4.3	4.0
SD	2.02	3.03	2.50
Minimum	1	1	1
Median	3.5	4.0	4.0
Maximum	6	12	12
Epilepsy nurse contact			
n (%)	22 (84.6)	23 (92.0)	45 (88.2)
At least one contact, *n (%)*	12 (46.2)	12 (48.0)	24 (47.0)
Missing, *n (%)*	4 (15.4)	2 (8.0)	6 (11.8)
Number of contacts (if used)[a]			
Mean	2.4	2.1	2.3
SD	1.37	1.56	1.45
Minimum	1	1	1
Median	2.0	1.5	2.0
Maximum	6	6	6

a Mean, SD, minimum, median and maximum number of attendances calculated for those with at least one attendance or contact.

Emergency department use in 12 months prior to enrolment

Hospital Episode Statistics emergency department data

Hospital Episode Statistics ED data for the 48 patients for whom consent were maintained over the trial show that they together made 122 ED visits in the 12 months before randomisation. Frequency of ED use among them was positively skewed (*Figure 5*). The median number of visits was 2 (range 0–12) (see *Table 12*).

As described in *Chapter 3*, patient identification centred on the use of NHS ED attendance records and only patients who, when telephoned, said that they had made two or more ED visits for epilepsy in the prior 12 months were recruited. Despite this process, data from the HES system indicated that four (8.3%) patient participants had not made any ED visits during the 12 months prior to recruitment and a further 19 (39.6%) were noted to have made only one ED visit.

Self-reported emergency department data

Self-reported data were available for 45 (88.2%) patient participants. The median number of visits was four (range 0–107) (see *Table 12*). Again, despite the screening processes, four (8.9%) patient participants responded on the questionnaire completed subsequent to telephone screening that they had not made any visits during the prior 12 months and 3 (6.7%) reported that they had made only one visit.

Relationship between Hospital Episode Statistics and self-reported data

There were 42 patient participants who had self-reported ED data at baseline (T0) and for whom consent remained in place for obtaining their HES ED data. Bland–Altman plots of the agreement between self-reported and HES data on ED visits were produced.

Primary focus is given to the plot shown in *Figure 6*. This is based on data from 41 rather than 42 patient participants. This is because the distribution of self-reported ED use was particularly influenced by one patient participant who self-reported 107 visits in the prior 12 months. We can confirm that that report of 107 visits was checked against the participant's answer on the questionnaire and did not reflect a data entry error. Given that only one ED visit in the 12 months was recorded for this patient participant in HES data, we considered the self-report of 107 ED visits to be an outlier and excluded this in the plot shown in *Figure 6* (*Appendix 14* presents a Bland–Altman plot without any exclusions).

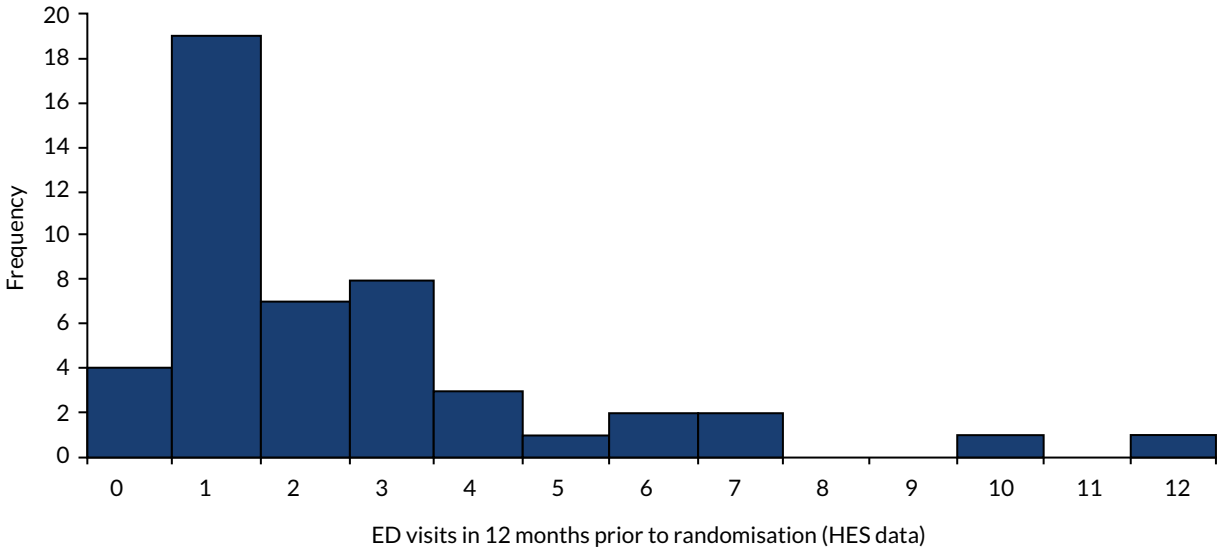

FIGURE 5 Histogram of the number of ED attendances in the previous 12 months by patients according to HES system.

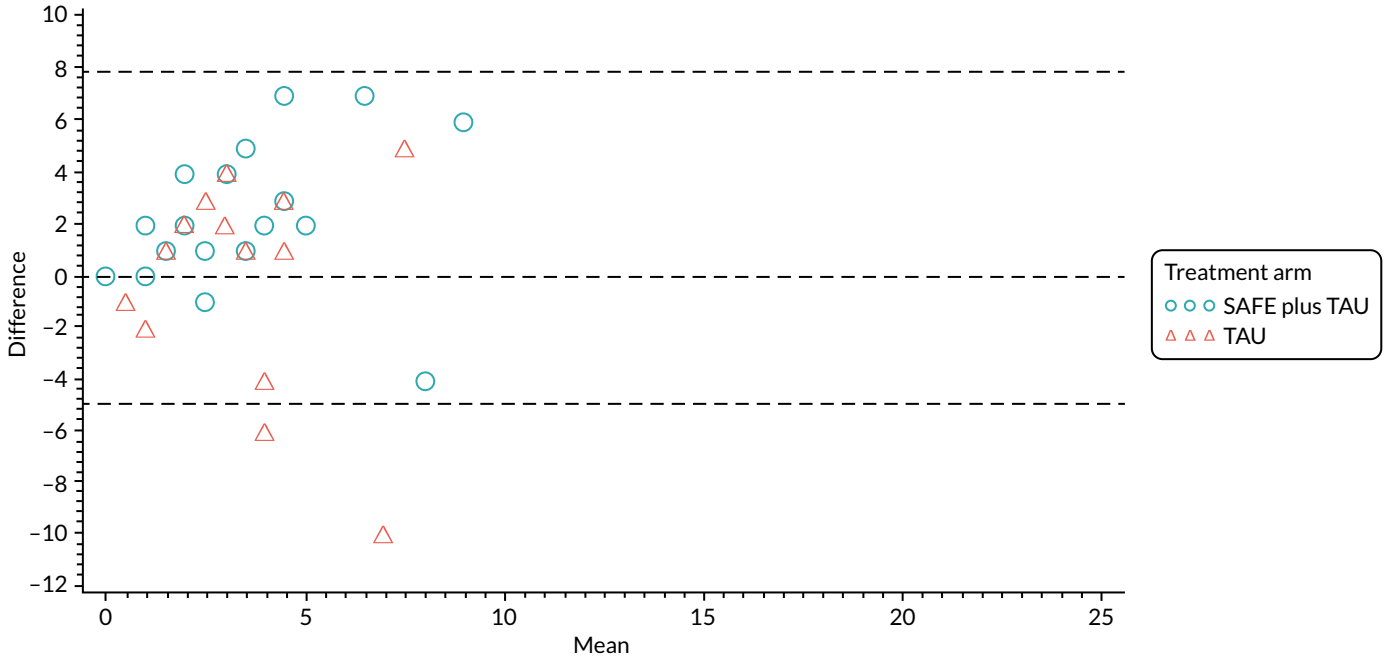

FIGURE 6 Bland–Altman plot of agreement between self-reported and HES data on ED visits at baseline ($n = 41$; excludes outlier).

Figure 6 shows that disagreement existed between self-reported and HES data for most patient participants. Most (76.2%) participants self-reported more ED visits than were indicated by the HES system. Only three (7.1%) participants reported the same number of ED visits as were recorded by HES. *Figure 6* shows that the limit of agreement was −5.0 visits (i.e. five fewer visits in self-reported data than in HES data) to 7.7 visits (i.e. 7.7 visits more in self-reported data than in HES data).

Psychosocial measures

Compared with a maximum possible score of 100, the mean QOLIE-31-P score was 48.3 (SD 17.3), with a large range (17.1–79.5). Twenty-six (50.9%) participants had 'probable' anxiety and 11 (21.6%) had 'probable' depression. Assessment of self-stigma revealed that most ($n = 42$; 82.3%) felt at least some stigma because of epilepsy and 15 (29.4%) felt highly stigmatised.

Comparability of treatment arms, including in emergency department use

Considering the small sample size, the process of randomisation was largely successful in generating two treatment arms broadly similar in demographics and scores on the baseline assessment tools (see *Tables 11* and *12*). Some differences were apparent in their ED use prior to randomisation (as measured by HES and self-report); ED use was slightly higher in the TAU arm than in the SAFE plus TAU arm (see *Table 12*).

Representativeness

The age, sex and social deprivation profile of the randomised patient participant sample was compared with that of the patients who were eligible to participate but who declined to participate or were not contactable. This showed that the two groups were comparable in age and social deprivation profile but that females were slightly over-represented in the recruited sample (*Table 13*).

Significant other participants

Most (72.5%) patient participants took part in the trial with a SO. SOs were typically a partner or spouse (43.2%), a parent (21.6%), or a son or daughter (16.2%). Most (75.5%) SOs lived in the same household as the patient and had contact with them every day of the week (89.2%). Their mean age was 43.2 years (SD 17 years, range 17–79 years) and most (59.5%) were female. Among the SOs, 32.4% reported having a medical condition themselves.

Anxiety levels among SOs were high, with 15 (40.5%) of the SOs having a score indicating 'probable' clinical anxiety. Only three (8.1%) had a score indicating 'probable' clinical depression. The mean Zarit caregiver burden score[170] was 18.9 (SD 12.51), with most being categorised as reporting either little or no burden ($n = 23$; 62.2%) or mild to moderate burden ($n = 11$; 29.7%). Further characteristics of the SOs, including by treatment arm, are provided in *Appendix 15*.

Researcher unblinding

The researcher correctly stated the treatment allocation of 35 out of the 51 patient participants, giving a rate of unblinding of 68.6% (95% CI 54.1% to 80.9%). The chance-corrected Cohen's kappa statistic for this level of agreement is 0.37 (95% CI 0.12 to 0.63), indicating 'fair' agreement. For SO participants, the researcher correctly stated the treatment allocation of 24 out of the 36 SOs (estimate missing for one SO), giving a rate of unblinding of 66.7% (95% CI 49.0% to 81.4%) and a Cohen's kappa statistic for agreement of 0.33 (95% CI 0.02 to 0.64). For only three (5.8%) patient participants and three (8.3%) SO participants did the researcher report that they strongly thought that they knew the patient participant's treatment allocation because of comments participants had made.

Summary

A successful pilot trial was completed in terms of a largely representative sample being recruited and randomised and most patients randomised to SAFE receiving it. There were no protocol deviations and the research worker completing the outcome assessments remained blind to treatment allocation.

TABLE 13 Demographic characteristics of eligible participants by agreement to participate in the trial

Demographic characteristic	Agreed to participate	Did not agree to participate
Sex*, n *(%)	***(N = 51)***	***(N = 379)*[a]**
Male	22 (43.1)	192 (50.7)
Female	29 (56.9)	187 (49.3)
Missing	0 (0.0)	0 (0.0)
Age (years) at presentation to the ED		
n (%)	51 (100.0)	379 (100.0)
Mean, years	39.9	40.6
SD, years	15.66	16.83
Minimum, years	16.4	16.2
Median, years	38.8	37.5
Maximum, years	71.3	84.4
Missing, *n (%)*	0 (0.0)	0 (0)
***IMD*[b]**	***(N = 51)***	***(N = 379)***
Decile 1		
n (%)	25 (49.0)	188 (49.6)
Minimum rank	44	28
Median rank	673.0	924.5
Maximum rank	3202	3107
Deciles 2 and 3		
n (%)	13 (25.4)	82 (21.6)
Minimum rank	3989	3291
Median rank	6785	5309
Maximum rank	8281	9835
Deciles 4–6		
n (%)	6 (11.8)	59 (15.6)
Minimum rank	9881	10,277
Median rank	11,924	14,459
Maximum rank	16,004	19,659
Deciles 7–10		
n (%)	6 (11.8)	50 (13.2)
Minimum rank	24,971	19,826
Median rank	28,876	22,673
Maximum rank	32,724	32,396
Decile missing		
n (%)	1 (2.0)	0 (0)

a Includes seven patients who could not be contacted owing to an incorrect postal address and two patients who were not sent an invite letter in error.
b Decile and rank missing for one recruited participant because they resided in Wales. The IMD ranks every small area in England from 1 (most deprived area) to 32,844 (least deprived area).

However, only one of the two predetermined 'stop/go' criteria for a definitive trial was met. Specifically, the criterion of securing primary outcome data for $\geq$ 75% of participants was satisfied (in that it was secured for 94%), but the criterion regarding the percentage of eligible patients agreeing to participate was not: only 12.5% rather than $\geq$ 20% agreed to take part. The low consent rate, as well as fewer patients being found to be eligible to take part and contactable than anticipated, meant that the target sample size for the pilot RCT was not achieved. The pilot RCT also revealed that identifying patients from local ED records could be resource intensive and that securing routine outcome data on ED use via the HES system requires substantial time.

Chapter 5 Intervention fidelity

Introduction

Seizure first Aid training For Epilepsy is a group-based intervention comprising multiple interacting components and requires a number of behaviours on behalf of those delivering and receiving SAFE. These features create opportunity for variation in its delivery. To permit accurate interpretation of the estimates of its effect generated by the pilot RCT, as well as to help determine whether or not SAFE can be delivered as intended in a trial context, information on its implementation fidelity in the pilot RCT is required. Implementation fidelity refers to the extent to which the core content of SAFE was delivered (adherence) as intended and with what sort of skill (competency). Such monitoring is recommended by the Template for Intervention Description and Replication (TIDieR) extension to the CONSORT statement.[187]

Assessing for both adherence and competence is important because the two are not necessarily equivalent (e.g. a facilitator can be highly adherent to treatment manual procedures but not be competent in deploying them). An aspect of competence that appears important when delivering group-based complex interventions[155] is interactivity between facilitator and recipients – namely, the degree of 'didacticism'.[155,188] Although some didacticism is needed to ensure that certain information is provided and participants remain oriented to the goals of the intervention, interaction means that participants are asking questions and obtaining clarification and so are ensuring that the intervention is tailored to their needs. It also permits participants to share and learn from one another.

In the light of the above information, we therefore report how we (1) developed a measure of adherence for SAFE and evaluated its reproducibility, (2) used an existing method for assessing didacticism and evaluated its reproducibility when applied to SAFE and (3), using audio-recordings of intervention sessions, determined the extent of adherence and didacticism demonstrated in the delivery of SAFE in the pilot RCT.

Methods

All seven courses run for the SAFE plus TAU arm of the pilot RCT were audio-recorded and assessed for implementation fidelity. Because SAFE is brief and it is not known which components are its key, active, behaviour-changing ingredients, all parts of SAFE were evaluated for their fidelity. The facilitator was aware that course recordings were to be rated.

Developing the intervention fidelity measurement instruments

Adherence

A checklist of SAFE's intended content was developed on the basis of the facilitator's manual (see *Report Supplementary Material 1*), which lists the 37 items that were meant to be delivered across SAFE's six modules. The checklist asked a rater to report the extent to which each item was delivered (0 = not delivered; 1 = partially delivered; 2 = fully delivered).

The number of items in each module differed (range 4–10). To allow adherence in the different course modules to be compared, average adherence ratings were calculated.

Competence

The intention was that learning would be elicited rather than taught via SAFE, with the behaviour of the educational facilitator seeking to promote a non-didactic approach. It was not known what level of didacticism represented the optimum and would be associated with the greatest improvement in patient outcomes. It was nevertheless important to gauge what balance between adherence and didacticism was being achieved when SAFE was being delivered in the pilot.

Therefore, using a method previously developed by our team,[189] didacticism was assessed using Eudico Linguistic Annotator 5.1 software (Max Planck Institute for Psycholinguistics, Language Archive, Nijmegen, Netherlands).[190] This software permitted a rater to listen to the audio-recording of a SAFE course and simultaneously code when the facilitator was speaking. The total amount of facilitator speech, as a proxy measure of how didactic the course was, was then calculated. This was divided by the duration of the course to generate the percentage of course time during which the facilitator was speaking. Filler words (e.g. 'oh', 'OK' and 'yeah') were not considered instances of facilitator speech.

Testing the measures

To assess reliability of the implementation fidelity measures, two independent raters individually evaluated each course using the fidelity measures. The raters were final-year students completing a Bachelor of Science degree in psychology. Their training consisted of completion of practice adherence and didacticism ratings on two courses not delivered as part of the trial.

Data analysis

Testing the measures

Inter-rater agreement was calculated using MedCalc 18.2.1 (MedCalc Software Ltd, Ostend, Belgium). The intraclass correlation coefficient[191] evaluated agreement between the two raters' didacticism ratings. For the adherence measure, the ratings from the two raters were tabulated and simple percentage agreement first calculated. Inter-rater reliability was then assessed using the chance-corrected weighted kappa statistic.

Because paradoxical values of kappa can occur owing to bias or skewed prevalence,[192] the influence of these factors was considered by calculating a prevalence index and a bias index and by comparing the change in kappa when the prevalence-adjusted bias-adjusted kappa for ordinal scales (PABAK-OS) was calculated using a PABAK-OS calculator (URL: www.singlecaseresearch.org/calculators/pabak-os; accessed 27 August 2019). The prevalence index can range from −1 to 1 (0 indicates equal probability) and the bias index ranges from 0 to 1 (0 indicates equal marginal proportions and so no bias).[193]

Course fidelity

The raters' adherence and didacticism scores for each course were averaged and described using descriptive statistics.

Results

Testing the fidelity instruments

Adherence scale: inter-rater reliability

For 96% of adherence items, the raters made the same judgement about the extent to which the item was delivered but the weighted kappa statistic was only 0.66 (95% CI 0.50 to 0.83). This was a consequence of prevalence bias (–0.83; bias index 0.06), with 94.6% of the raters' ratings using the category 'fully delivered'. Given this, the PABAK-OS statistic of 0.91 (95% CI 0.85 to 0.97) (which equates to 'substantial agreement') provided a more accurate reflection of rater concordance.

Didacticism measure: inter-rater reliability

With a coefficient of 0.96 (95% CI 0.78 to 0.99), the intraclass correlation coefficient indicated that the two raters' judgements regarding didacticism were highly correlated.

Course fidelity

Adherence

Adherence was high. Among the 259 items meant to be delivered across the seven courses, 228 (88.0%) were 'fully delivered'. Only eight (3.1%) were 'not delivered' (*Table 14*). The average adherence rating (with a maximum of 2) given to the items across the SAFE courses was 1.88 (SD 0.11, range 1.65–1.97) (see *Appendix 16*).

The mean and range of adherence scores given to the individual intervention items showed that no item proved too challenging to be fully delivered at least once. The mean score of only one intervention item (namely, requiring the facilitator to inform the participants about when the demonstrated recovery position should and should not be delivered) fell below 1 (i.e. to 0.79).

Didacticism

The mean percentage of facilitator speech across the courses was 55% (SD 5.4%), with a range of 49–64% (see *Table 14*).

Summary

The SAFE intervention was found to have been delivered as intended across the pilot RCT. The adherence measure indicated that the facilitator delivered almost all the items prescribed by the treatment manual. Moreover, they were able to do this while maintaining a high degree of interactivity. In the light of these findings, we do not expect the estimate of intervention effect found in the pilot RCT to be influenced by poor implementation fidelity.

TABLE 14 Characteristics of the courses

Course number	Adherence rating		Didacticism rating: percentage (SD) of time facilitator speaking
	Number (%) of items fully delivered	M rating (SD) across 37 items	
1	35 (94.6)	1.97 (0.11)	54.45
2	33 (89.2)	1.91 (0.35)	57.57
3	33 (89.2)	1.92 (0.25)	63.94
4	35 (94.6)	1.95 (0.22)	54.48
5	32 (86.5)	1.86 (0.40)	49.59
6	27 (73.0)	1.65 (0.69)	48.87
7	33 (89.2)	1.88 (0.39)	59.42
Across all seven courses	228 (88.0)	1.88 (0.11)	55.47 (5.35)

Each course consisted of six modules. Together these contained 37 items that were to be delivered. The extent of each of these items delivered was rated using the following scale: 0 = item not delivered; 1 = item partially delivered; 2 = item fully delivered.

Chapter 6 Outcomes of the pilot randomised controlled trial and implications for a definitive trial

Introduction

Primary and secondary outcome measures were captured/completed to varying degrees at baseline and at 3-, 6- and 12-month follow-up. This chapter outlines the findings from these assessments.

Outcome measures

Proposed primary outcome: emergency department use measured by the Health Episode Statistics system

Routinely collected data on ED use from the HES system were secured for 48 (94.1%) of the randomised patient participants. The mean number of visits recorded over the 12 months following randomisation to the SAFE plus TAU arm was 1.8 (SD 3.14) and the median was 1 (range 0–12). For the TAU arm, the mean was 3.4 (SD 4.78) visits and the median was 2 (range 0–20) visits. Compared with the 12 months prior to randomisation, mean ED use over the follow-up period reduced for the SAFE plus TAU arm by 0.3 (28%) visits. For the TAU arm, it increased by 0.4 (11%) visits over the follow-up period (*Table 15*).

Emergency department use was overdispersed. However, there was not an excess of zeros (Vuong's test:[180] $z = -0.17$; $p = 0.87$). For this reason, NBR compared the effect of treatment arm on ED use, which showed that the estimated rate of ED visits following randomisation was around 46% lower in the SAFE plus TAU arm than in the TAU arm (rate ratio = 0.54). This difference was not statistically significant at the 5% alpha level (95% CI 0.24 to 1.18), nor at the 10% level (90% CI 0.28 to 1.04). The difference was statistically significant at the 20% level (80% CI 0.32 to 0.90; $p = 0.12$) (*Table 16*).

Owing to a slight imbalance between treatment arms in ED use in the 12 months prior to randomisation (i.e. ED visits at baseline), we also applied an adjusted NBR, including SAFE plus TAU arm and baseline ED visits. The results showed that an increased number of ED visits pre randomisation was associated

TABLE 15 Number of ED visits patient participants made according to HES data

	Treatment arm		
Number of ED visits	SAFE plus TAU	TAU	Total
During the 12 months prior to baseline			
n (%)	25 (96.2)	23 (92.0)	48 (94.1)
Mean	2.1	3	2.5
SD	2.22	2.76	2.51
Minimum	0	1	0
Median	1	2	2
Maximum	10	12	12
Missing, *n (%)*	1 (3.8)	2 (8.0)	3 (5.9)

continued

TABLE 15 Number of ED visits patient participants made according to HES data (*continued*)

Number of ED visits	Treatment arm		Total
	SAFE plus TAU	TAU	
During the 12 months following randomisation			
n (%)	25 (96.2)	23 (92.0)	48 (94.1)
Mean	1.8	3.4	2.6
SD	3.14	4.78	4.05
Minimum	0	0	0
Median	1	2	1
Maximum	12	20	20
Missing, *n (%)*	1 (3.8)	2 (8.0)	3 (5.9)
Change from baseline at 12 months			
n (%)	25 (96.2)	23 (92.0)	48 (94.1)
Mean	−0.3	0.4	0.1
SD	1.99	3.81	2.99
Minimum	−4	−5	−5
Median	0	0	0
Maximum	5	16	16
Missing, *n (%)*	1 (3.8)	2 (8.0)	3 (5.9)

TABLE 16 Differences between groups in number of HES-recorded ED visits: SAFE plus TAU vs. TAU alone

Model and parameter	Value	CI			*p*-value
		95%	90%	80%	
12 months following randomisation[a]					
Negative binomial					
SAFE plus TAU, rate ratio	0.54	0.24 to 1.18	0.28 to 1.04	0.32 to 0.90	0.12
Dispersion parameter	1.53	0.67 to 2.39	0.80 to 2.25	0.96 to 2.09	NA
Vuong's test[b]	−0.17	NA	NA	NA	0.87
12 months following randomisation with adjustment for baseline ED visits					
Negative binomial					
SAFE plus TAU, rate ratio	0.62	0.33 to 1.17	0.36 to 1.06	0.41 to 0.94	0.14
Baseline ED visits, rate ratio	1.33	1.18 to 1.52	1.20 to 1.49	1.23 to 1.45	< 0.001
Dispersion parameter	0.69	0.17 to 1.21	0.26 to 1.13	0.35 to 1.03	NA
Vuong's test[b]	−0.13	NA	NA	NA	0.90

NA, not applicable.
a Analysis based on 48 patient participants.
b Vuong's test[180] *p*-value interpretation: a significantly negative parameter value favours the negative binomial model and significantly positively favours the zero-inflated negative binomial model. A non-significant value indicates no significant difference between the models; therefore, the simpler negative binomial model is preferred.

with an increased number of post-randomisation ED attendances (rate ratio 1.33, 95% CI 1.18 to 1.52). With the adjustment, the estimated effect size for treatment arm reduced, with the rate of ED visits for the SAFE plus TAU arm being around 38% lower than that for the TAU arm (rate ratio 0.62). In this adjusted analysis, treatment arm was not significantly associated with ED use at the 5% (95% CI 0.33 to 1.17) or 10% (90% CI 0.36 to 1.06) level; the treatment arm was statistically significant at the 20% level (80% CI 0.41 to 0.94; $p = 0.14$).

Secondary outcome data

Emergency department use: self-reported

Self-reported data on ED use during both the 12 months prior to and the 12 months following randomisation were available for 34 (66.6%) of the randomised patient participants. The mean number of ED visits reported by patient participants in the SAFE plus TAU arm was 1.2 and the median was 0.0. The mean number of ED visits reported by patient participants in TAU arm was 2.9 and the median was 1.0. Compared with the 12 months prior to randomisation, mean ED use over the follow-up period reduced by 2.6 visits for participants in the SAFE plus TAU arm. For the TAU arm, this reduced by 0.3 visits (see *Appendix 17*).

Negative binomial regression with (rate ratio 0.34, 95% CI 0.11 to 1.07; $p = 0.10$) and without (rate ratio = 0.42, 95% CI 0.15 to 1.20; $p = 0.06$) adjustment for ED use over the 12 months prior to randomisation indicated that the estimated rate of ED visits following randomisation was around 66% and 58% lower in the SAFE plus TAU arm and in the TAU arm, respectively (*Table 17*).

Relationship between Hospital Episode Statistics and self-reported data

Among the 34 patient participants who had self-reported ED data at 12 months (T3) and for whom consent remained in place and HES data were secured, 11 (32.4%) had the same number of ED visits recorded in HES and self-reported data: seven (41.2%) from the TAU arm and four (23.5%) from the SAFE plus TAU arm. A total of 13 patient participants (38.27%) had more ED visits recorded in HES data than in self-reported data and 10 (29.4%) self-reported more ED visits than were recorded by HES data; proportions were similar across the two treatment arms (*Table 18*).

TABLE 17 Differences between groups in number of self-reported ED visits: SAFE plus TAU vs. TAU alone

		CI			
Model and parameter	**Value**	**95%**	**90%**	**80%**	***p*-value**
12 months following randomisation					
Negative binomial					
SAFE plus TAU, rate ratio	0.42	0.15 to 1.20	0.17 to 1.01	0.21 to 0.83	0.10
Dispersion parameter	1.85	0.50 to 3.20	0.72 to 2.98	0.97 to 2.73	NA
Vuong's test[a]	0.49	NA	NA	NA	0.62
12 months following randomisation with adjustment for baseline ED visits					
Negative binomial					
SAFE plus TAU, rate ratio	0.34	0.11 to 1.07	0.13 to 0.88	0.16 to 0.72	0.06
Baseline ED visits, rate ratio	1.15	0.83 to 1.60	0.88 to 1.52	0.93 to 1.43	0.39
Dispersion parameter	1.87	0.38 to 3.36	0.62 to 3.12	0.89 to 2.84	NA
Vuong's Test[a]	−0.13	NA	NA	NA	0.90

NA, not applicable.

a Vuong's test[180] *p*-value interpretation: a significantly negative parameter value favours the negative binomial model and significantly positively favours the zero-inflated negative binomial model. A non-significant value indicates no significant difference between the models; therefore, the simpler negative binomial model is preferred.

TABLE 18 Comparison of HES-recorded and self-reported ED visits during the 12 months post randomisation

HES-recorded vs. self-reported ED visits	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
More HES recorded than self-reported	7 (41.2)	6 (35.3)	13 (38.2)
Equal	4 (23.5)	7 (41.2)	11 (32.4)
More self-reported than HES recorded	6 (35.3)	4 (23.5)	10 (29.4)

Figure 7 shows a Bland–Altman plot of the agreement between the mean number of self-reported and HES-recorded ED visits for the 34 patient participants; the limits of agreement were −5.3 visits (i.e. 5.3 fewer visits recorded in self-reported data than in HES data) to 4.4 visits (i.e. 4.4 visits more recorded in self-reported data than in HES data). Compared with baseline (see *Figure 6*), this Bland–Altman plot demonstrates a relatively even spread of self-reported versus HES-recorded ED visits.

Other secondary outcome measures

As per the statistical analysis plan, differences between the two treatment arms on the remaining secondary outcome measures were not formally statistically tested. For completeness, summary statistics for the arms on these measures at 6 months' (T2) and 12 months' (T3) follow-up are reported in *Appendix 18*.

Safety and adverse events

A total of 18 (35.3%) patient participants reported adverse events over the course of their follow-up (see *Appendix 19*). In the SAFE plus TAU arm, six adverse events were reported by six participants; 13 adverse events were reported by 12 participants in the TAU arm. Only one SAE occurred during the study: a diagnosis of previous status epilepticus. This was reported by one SAFE plus TAU arm participant. On medical review, it was considered unlikely to be related to SAFE or participation in the trial because it arose from investigations that the participant had been having before they began participating in the trial.

Participant feedback

A total of 32 (68.1%) patient participants and 20 (62.5%) SOs completed the participant feedback questionnaire at 12 months (T3). All but one said that they would participate in the trial again (*Tables 19* and *20*).

When asked to explain why, the limited burden associated with participating was mentioned, as was a sense of duty to help improve things for others. Some SAFE plus TAU arm participants mentioned the benefit they perceived themselves to have derived from SAFE. Illustrative quotes included the following:

> *I found that the study was not an issue or an inconvenience and I was happy to participate and would happily take part in any future studies.*
>
> *PWE participant*

> *I'm more than happy to help in a study that helps towards epilepsy.*
>
> *PWE participant*

> *Before we done it [participated in the research] we didn't have a clue [. . .] Sometimes we would have gone to the hospital if we needed [. . .] but now we don't need to go.*
>
> *SO*

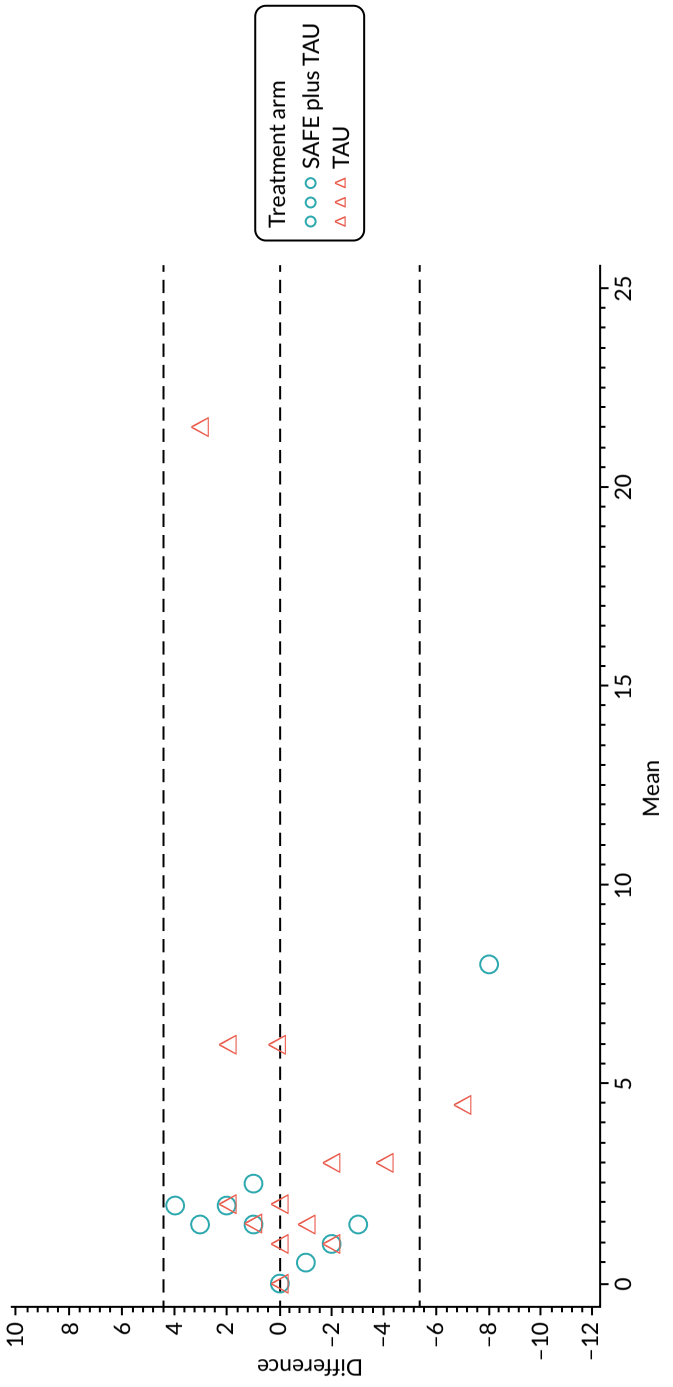

FIGURE 7 Bland–Altman plot of agreement between self-reported and HES-recorded ED visits at 12 months ($n = 34$).

TABLE 19 Feedback on participation in the SAFE trial: patient participants

Feedback on participation in the SAFE trial	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
If time suddenly went backward, and you had to do it all over again, would you agree to participate in the trial?	***(N = 26)***	***(N = 25)***	***(N = 51)***
Definitely yes	15 (57.7)	10 (40.0)	25 (49.0)
Probably yes	2 (7.7)	4 (16.0)	6 (11.8)
Probably no	0 (0.0)	1 (4.0)	1 (2.0)
Definitely no	0 (0.0)	0 (0.0)	0 (0.0)
Not sure	0 (0.0)	0 (0.0)	0 (0.0)
Missing	9 (34.6)	10 (40.0)	19 (37.2)

TABLE 20 Feedback on participation in the SAFE trial: SO participants

Feedback on participation in the SAFE trial	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
If time suddenly went backward, and you had to do it all over again, would you agree to participate in the trial?	***(N = 18)***	***(N = 19)***	***(N = 37)***
Definitely yes	11 (61.1)	9 (47.4)	20 (54.1)
Probably yes	0 (0.0)	0 (0.0)	0 (0.0)
Probably no	0 (0.0)	0 (0.0)	0 (0.0)
Definitely no	0 (0.0)	0 (0.0)	0 (0.0)
Not sure	0 (0.0)	0 (0.0)	0 (0.0)
Missing	7 (38.9)	10 (52.6)	17 (45.9)

Some participants provided comments relating to recruitment. No concerns were raised regarding randomisation, indicating that the process was acceptable. A point made by a number of participants was that, although they valued the intervention, they felt the offer seemed somewhat reactive and that a more preventative approach to self-management support might be valuable. They said that taking part in SAFE had been their primary source of education since being diagnosed, with health-care encounters having previously focused on 'medication and never about education or management' (SO participant) and that there was a need to offer such an intervention to those who have been recently diagnosed with epilepsy.

In terms of continued participation in the trial, a number of participants reported that they had experienced challenges in completing the questionnaires during the course of the study owing to instances of being unwell. Several participants from the TAU arm noted that memory problems and the gap between data collection episodes meant that they had forgotten about their participation in the study and so their motivation to take part when contacted had reduced.

Sample size calculation for future trial

The proposed primary outcome measure for a definitive trial is ED use as measured by HES. The pilot RCT found a reduction of around 47% in ED use in the SAFE plus TAU arm in the 12 months following randomisation compared with the TAU arm.

Table 21 shows the number of patient participants that would be required per arm for a definitive trial. Depending on the estimate of the dispersion parameter from the pilot trial that is used and the statistical power required, the number of patient participants needed per arm in a definitive trial ranges from 123 to 451.

If the central value of the estimate range for the dispersion parameter (k) of 0.69 is used, 90% power stipulated and 9.4% of recruited patients eventually withdraw consent to access their HES data (as observed in the pilot), a sample of 674 patients [(308 × 2) + 58] would need to be recruited for a definitive trial of SAFE. Using the estimates for eligibility and consent from the pilot trial, it would be anticipated that the triage cards of > 51,000 patients would need to be screened and > 7000 patients invited to secure a sample of 674 patients.

For the pilot RCT, three type 1 EDs acted as recruitment sites. These EDs generated, on average, 17.6 patient accruals each from 19 months of attendances (i.e. ≈ 1 per month). The EDs were similar in size to EDs in England, with the mean number of attendances (for any reason) being in line with the average for English EDs.[194] It can therefore be estimated that a definitive trial would require around 39 average-sized ED sites to recruit the necessary sample. This would equate to about half of England's type 1 EDs.

Summary

Using data from the 94% of patient participants on whom primary outcome data were secured, estimates for the effect of SAFE plus TAU on ED use were generated. Feedback from participants on trial participation was also secured. Participation in the trial was not associated with adverse effects and participants for the most part welcomed taking part and receiving the intervention. Using the estimate of effect and evidence from the pilot RCT on eligibility and uptake, it was calculated that a large definitive trial, in terms of recruitment sites and starting sample, would be needed to definitively judge the efficacy of the SAFE intervention.

TABLE 21 Required sample size for a definitive trial to detect estimated effect of SAFE plus TAU on ED use (measured using HES data)

	≈ 47% reduction (from 3.4 to 1.8 visits) in 12 months compared with TAU	
Dispersion parameter (k)	n per arm ($\alpha = 0.05$; 80% power; $\beta = 0.2$)	n per arm ($\alpha = 0.05$; 90% power; $\beta = 0.1$)
0.17	123	164
0.5	191	255
0.69	230	308
1	293	393
1.21	337	451

Dispersion parameter taken from the adjusted NBR model in the pilot RCT ($k = 0.69$, 95% CI 0.17 to 1.21). See *Table 16*.

Chapter 7 Economic evaluation

Introduction

When the feasibility of a definitive trial is being considered, an important part of the decision calculus is the cost of delivering the intervention to be trialled. Cost is important because it will affect the ease with which 'excess treatment costs' can be secured and would be fundamental to future cost-effectiveness analysis. It is also important because stakeholders will want to consider the budget impact and scalability of the intervention to be tested should it be found to be cost-effective. In contrast to health technologies, the costs of complex interventions such as SAFE are often less well characterised and may vary depending on the context of use. Microcosting is a method that provides detailed, bottom-up cost data based on each component of the delivery of an intervention.[195]

We performed a microcosting to calculate the fixed and variable costs of delivering SAFE in the context of the pilot RCT. The cost of developing the SAFE intervention via the processes described in *Chapter 2* was also determined. Such information is rarely provided but can be helpful for those planning similar endeavours and for research funders.

Methods

The microcosting adopted the perspective of an academic non-profit-making institution and was conducted in three stages: (1) identification of resources; (2) measurement; and (3) valuation.[196]

Step 1: identification of resources

A health economics researcher (EH) met with staff central to the development of the SAFE intervention (academic staff AN and DS) and delivery (epilepsy nurse specialist and SAFE facilitator Juliet Bransgrove and project administrator Gail Moors; see *Acknowledgements*) to map out the courses run for the project. The work and resources required for each were attributed to one of three categories according to the primary purpose of the course: inform intervention design, participants in the SAFE plus TAU arm and participants in the TAU only arm (*Figure 8*).

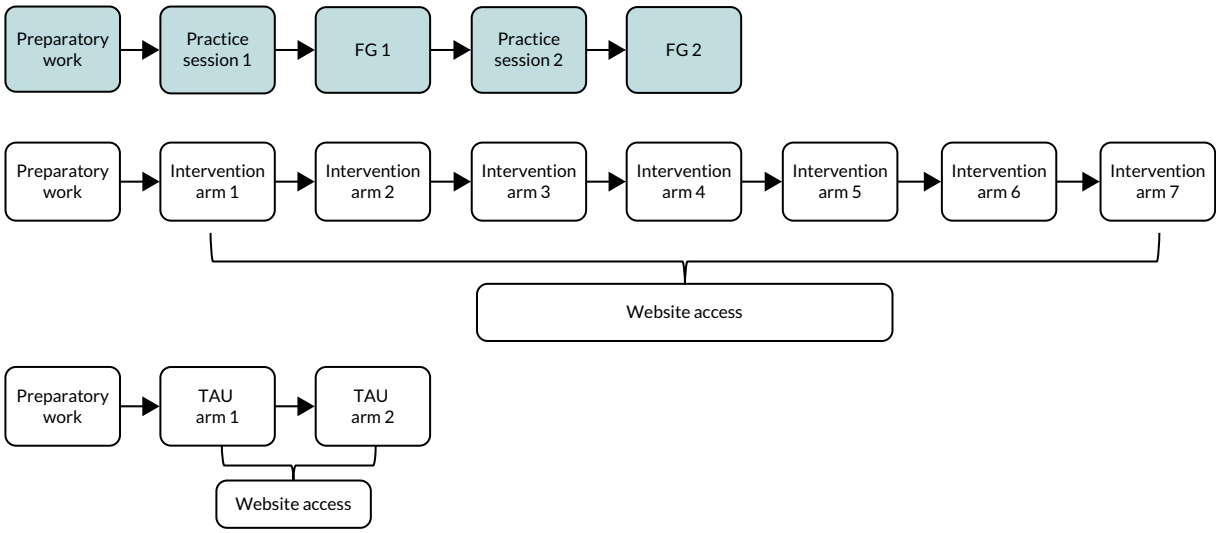

FIGURE 8 Workflow. Light blue shading signifies research and development.

The resources and items required to deliver SAFE were also differentiated as fixed or variable. Fixed resources were constant regardless of the number of people attending the course (e.g. room hire, facilitator). Variable resources were those that changed depending on the number of attendees (e.g. patient/SO take-away information packs, travel expenses). Participant involvement was costed from the point at which they were invited to attend a SAFE session to more accurately reflect routine practice.

Step 2: measurement

The quantity of use of the resources identified in stage 1 was measured. To capture this information we used the 'time and motion method'.[197] This involved the completion (by AN, DS, Juliet Bransgrove and Gail Moors; see *Acknowledgements*) of electronic data collection forms on which they self-reported the time that they dedicated to different activities. The research team (AN and DS) also recorded details of the number of participants invited and attending each of the SAFE sessions and non-staff resources.

Staff time and costs

Time was split into preparatory work (time in meetings, designing the SAFE intervention, administration of SAFE's content, planning and organising practice sessions, attending practice sessions, reviewing and editing SAFE's content) and programme delivery (time spent inviting participants, organising and attending SAFE sessions, packing up, and administration of participant expenses and the website). Staff recorded their time against each task for each SAFE session.

Travel time and costs

Staff involved in SAFE's delivery recorded estimates of time spent travelling to sessions and any travel costs. Travel costs were recorded for participants and taken from the study finance records as the total claimed per group.

Other costs

The two academic staff central to adapting the intervention (AN and DS) recorded all resources and items required to complete the activities identified in stage 1. This included office space for staff involved in course preparation and administration, telephone calls, stationery, printing and postage, leaflets for patients/SOs, advertising, participant remuneration (practice sessions only), venue hire, refreshments, equipment, and website domain and administration costs.

Step 3: valuation

A monetary value was attached to the quantities of resources used that were measured in step 2. Unit costs and details of suppliers were obtained using local data from the finance office of the University of Liverpool or national sources [e.g. Royal Mail (Royal Mail Group Ltd, London, UK)] as applicable (*Table 22*). Costs were calculated using price year 2017/18 and as Great British pounds. VAT was applied to equipment and consumables at a rate of 20%.

Details of staff job titles, employer and salary bands were obtained. Academic staff costs were calculated using University of Liverpool salary scales 2017/18 (hourly rates). Salary costs for the epilepsy nurse specialist delivering the training and the administrative assistant were calculated using hourly rates for casual workers and included 12.07% holiday pay. The epilepsy nurse specialist completed her role on the SAFE pilot study on an honorary contract with University of Liverpool at an hourly rate equivalent to band 6 in NHS England or Wales (Royal College of Nursing 2018). All salary costs were converted into cost per minute for the purpose of valuing time on activities. The staff costs per minute were multiplied by the time spent on each activity, then summed to obtain total staff costs.

Analysis

Resource use and costs were analysed to calculate the cost of developing the intervention, the fixed and variable costs of delivering the training sessions (SAFE plus TAU or TAU) and the mean cost per participant or patient (which includes the cost of attending with or without an SO). The cost of developing

TABLE 22 Unit costs

Category	Unit cost (£)	Source
Staff (per minute)		
Lecturer (grade 8)	0.46	University of Liverpool[198]
Administrative assistant	0.23	
Research fellow (grade 8)	0.40	
Epilepsy specialist nurse[a]	0.25	
IT technician (grade 8)	0.47	
Delegate expenses (per group)		
Practice group (travel)	55.00	Research study financial statement. Practice group remuneration: £10 shopping voucher per FG participant. Disaggregated travel expense data not available
Practice group (remuneration)	135.00	
SAFE plus TAU arm (travel)	40.00	
TAU arm (travel)	46.40	
Telephone (per minute, including VAT)		
Office line to UK mobile	0.06	BT (London, UK)[199]
Office line to UK landline	0.05	
Advertising (per advert)		
Practice group recruitment	45.00	*Liverpool Daily Echo* (Liverpool Daily Post & Echo Ltd, Liverpool, UK)
Venue costs		
Room hire (per course; 0.5 days, room capacity 20 delegates, includes PC and projector)	80.00	Royal Liverpool Academy[200]
Refreshments (per head; tea and coffee)	1.50	Royal Liverpool Academy[200]
Equipment (including VAT)		
Dictaphone (DM-650; Olympus, Tokyo, Japan) and boundary microphone (ME33; Olympus)	355.98	Research study financial statement
Study laptop	592.87	Desk Top Publishing Microsystems Ltd (Leeds, UK); purchased via University of Liverpool
Annual fees (including VAT)		
Website domain	20.94	Fasthosts Internet Ltd (Gloucester, UK)
Freepost licence fee	116.40	Royal Mail[201]
Delegate packs (including VAT)		
Invite pack (1 black and white, single-sided A4 page; envelope; second-class post; Freepost reply envelope)	1.12	Lyreco (Marly, France); University of Liverpool printing rates; Royal Mail
Reminder pack (1 black and white, single-sided A4 page; envelope; second-class post; Freepost reply envelope)	1.12	
FG consent form (1 black and white, single-sided A4 page)	0.04	

continued

TABLE 22 Unit costs (*continued*)

Category	Unit cost (£)	Source
Delegate booking confirmation (1 colour, double-sided A4 page; envelope; first-class)	0.80	
Delegate course pack (SAFE plus TAU) (slide handouts: 10 colour, single-sided A4 pages; certificate; folder)	0.89	
Delegate course pack (TAU) (slide handouts: 20 black and white, single-sided A4 pages; certificate; folder)	0.89	
Name badge	0.60	
Leaflet	1.00	ES
Convener pack[b] (4 acetates; 4 answer cards; 10 pens; flip chart; trainer manual;[c] clipboard;[c] 2 whiteboard markers;[c] 12 coloured marker pens[c])	4.96	Lyreco

IT, information technology; PC, personal computer.
a Epilepsy specialist nurse: honorary contract with University of Liverpool; ≈ band 6 in NHS England or Wales.
b Convener pack calculation uses mean cost per group.
c Single purchase, reused throughout 11 groups.

SAFE was calculated as the sunk cost of designing the intervention (incurred and independent of future training courses) plus the total fixed annual set-up cost. Calculations were based on an assumption of 11 groups per year and an equipment life of 1 year.

The epilepsy nurse specialist who facilitated the SAFE courses was not based locally but located in the region of the ES offices. This meant that she travelled to Liverpool to deliver the course. For this reason, a scenario analysis that excluded the travel time and travel expenses of the epilepsy nurse specialist facilitating the groups was conducted to explore a more realistic scenario of employing a local nurse.

The means and SDs of observed data were calculated. The 95% central range (CR) for costs and differences was generated using 10,000 bootstrap replications. All data were managed and analysed in Microsoft Excel® 2010 (Microsoft Corporation, Redmond, WA, USA).

Results

Over the course of the project, 11 SAFE intervention courses were run. Two were run to inform intervention design, seven were run for participants in the SAFE plus TAU arm and two were run after the trial was completed for the TAU arm. Data were collected from the four noted members of staff, with all data collection forms being complete and no missing data.

The total cost of developing the training was £9947, which included two practice SAFE courses attended by 27 people (*Table 23*); 88.72% of the development cost was a sunk cost independent of future training courses.

To deliver SAFE in the pilot RCT, the fixed cost (SAFE plus TAU arm or TAU arm) was £263 per group, which represented the cost of course facilitation and venue hire. The mean variable cost per group ($n = 9$) was £922 (SD £131, 95% CR £887 to £1085). There were no statistically significant differences in the mean cost per group between SAFE plus TAU and TAU only (SAFE plus TAU arm: mean £903, SD £134; 95% CR £760 to £1087; TAU arm: mean £986, SD £140, 95% CR £887 to £1085; difference in CR −£324 to £119).

TABLE 23 Total observed costs and cost per delegate to deliver SAFE

		SAFE delivery course										
				Treatment arm								
		Practice session		SAFE plus TAU							TAU	
Description	Design and set-up	1	2	1	2	3	4	5	6	7	1	2
Fixed costs (£)												
Equipment	928.85	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Website	77.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Freepost licence	116.40	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Venue	0.00	80.00	80.00	80.00	80.00	80.00	80.00	80.00	80.00	80.00	80.00	80.00
Facilitator (staff cost)	–	192.79	192.79	177.96	177.96	177.96	177.96	177.96	177.96	177.96	177.96	177.96
Facilitation resources	–	4.96	4.96	4.96	4.96	4.96	4.96	4.96	4.96	4.96	4.96	4.96
Total (fixed)	1122.37	277.75	277.75	262.92	262.92	262.92	262.92	262.92	262.92	262.92	262.92	262.92
Variable costs (£)												
Staff costs	4243.41	612.88	1158.56	591.19	521.84	429.37	429.37	318.41	318.41	318.41	299.96	416.03
Staff travel expenses	44.10	279.87	279.87	274.67	274.67	265.43	265.43	265.43	265.43	265.43	233.63	265.41
Participant expenses	0.00	180.00	200.00	40.00	40.00	40.00	40.00	40.00	40.00	40.00	92.80	0.00
Office costs (including telephone)	589.33	33.00	105.50	81.63	85.23	92.60	88.70	89.00	86.60	89.00	57.17	70.13
Stationery/print/postage	0.00	156.35	196.96	57.44	93.68	68.93	68.93	34.46	22.98	45.95	182.73	298.44
Refreshments	0.00	72.25	72.25	41.80	41.80	32.81	32.00	41.00	26.60	18.50	21.00	34.50
Advertising	45.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total (variable)	4921.84	1334.34	2013.13	1086.73	1057.22	929.13	924.42	788.30	760.01	777.29	887.28	1084.51

continued

TABLE 23 Total observed costs and cost per delegate to deliver SAFE (*continued*)

Description	Design and set-up	SAFE delivery course										
		Practice session		Treatment arm								
				SAFE plus TAU							TAU	
		1	2	1	2	3	4	5	6	7	1	2
Fixed and variable costs (£)												
Total	6044.21	1612.09	2290.88	1349.65	1320.14	1192.05	1187.34	1051.22	1022.93	1040.21	1150.20	1347.43
Delegates and arms												
Delegates (patient : SO ratio)	–	12	15	2 : 3	4 : 4	3 : 3	4 : 2	3 : 0	1 : 1	2 : 2	4 : 4	8 : 5
Mean cost (£) per delegate	–	134.34	152.73	269.93	165.02	198.68	197.89	350.41	511.47	260.05	143.78	103.65
Mean cost per arm, £ (SD; 95% CR)[a]				1166 (134.22; 1023 to 1350)								1249 (139.46; 1150 to 1347)
Mean cost per delegate, £ (95% CR)[a]				240 (211 to 278)								119 (110 to 128)
Mean cost per patient (with or without SO), £ (95% CR)[a]				408 (358 to 472)								208 (192 to 225)

a CRs generated from 10,000 bootstrap replications.
Two academic researchers, one epilepsy specialist nurse delivering the training, and administrative support.

On average, the TAU arms involved six more participants than the SAFE plus TAU arms. The mean cost per participant was £119 (95% CR £110 to £128) in the TAU arm; this was significantly lower than the cost per participant in the SAFE plus TAU arm, which was £240 (95% CR £211 to £278; difference in CR –£1137 to –£872); both estimates exclude fixed annual set-up costs of £1122.

The average ratio of patients to SOs was 3 : 2. The mean cost per patient (with or without SO) was £208 (95% CR £192 to £225) in the TAU arm; this was significantly lower than the cost per patient in the SAFE plus TAU arm, which was £408 (95% CR £358 to £472).

When including the cost of developing SAFE (£181 per person), the mean cost per participant, based on all 55 participants in SAFE plus TAU or TAU arms, was £375 (95% CR £348 to £402). This reduced to £214 (95% CR £188 to £241) when excluding sunk costs that would not be incurred again in the future.

Staff time accounted for 50.01% of the cost of the delivering SAFE and almost 70.21% of the development cost. Staff travel expenses accounted for an additional 21.10%. Travel expenses were high as a consequence of the specialist nurse delivering SAFE not being based locally.

Office, stationery, printing, postage and venue hire costs were relatively low. A scenario analysis of facilitator costs without travel expenses (time and cost) reduced the mean cost by 21.08%, from £194 (95% CR £167 to £221) to £152 (95% CR £124 to £179) per delegate or from £333 (95% CR £288 to £380) to £261 per patient.

Discussion

Delivering SAFE was estimated to cost £333 per patient (with or without a SO) and it is plausible that it could be delivered for as little as £261 per patient or £152 per delegate. The main cost contributors are staff costs and associated travel expenses and office costs. The annual fixed cost of setting up and running SAFE is £1122 (plus £35.07 per patient, based on 32 patients per year attending with or without a SO).

Chapter 8 Discussion

Principal findings

Part A: intervention development

A novel co-production approach enabled us to achieve our objectives of (1) optimising the content, delivery and behaviour change potential of the ES's existing course for PWE attending ED and their SOs and (2) developing a seizure management intervention that had support from representatives from the target service user population and from professional groups involved in their care.

The finalised intervention – SAFE – was brief, manualised, supported by the inclusion of a theory of behaviour change and based on a delivery method considered by stakeholders to be sustainable for the NHS. Feedback from service users who received the test version of the intervention was positive. This is despite it focusing on sensitive areas, such as potentially unnecessary hospital service by them and their own beliefs about epilepsy. Participants valued the straightforward guidance offered by SAFE and liked its group format. This concurs with previous observations, with PWE previously reporting that the format helps them 'feel less alone' and able to share and learn from others.[127] Our participants did identify potential barriers to intervention effect (e.g. memory difficulties) and we sought to ameliorate these (e.g. by providing participants with access to hard copies and online copies of the course materials).

Triallists have often been criticised for not describing complex interventions sufficiently for replication.[202] This is not the case for SAFE. Its content and the origin of each of its elements are clearly documented. A TIDieR checklist[187] is also available (see *Report Supplementary Material 2*).

The microcosting of intervention development activity is rare. At just under £10,000, the cost of developing SAFE is arguably low. This was, in part, because SAFE was adapted from an existing intervention and because the owners of the original course (the ES) did not charge for access to it or its materials. Our findings are important to disseminate because they could help those considering similar endeavours to accurately forecast activity, timelines and costs. They also provide funders with a benchmark against which to judge applications.

Part B: pilot randomised controlled trial

A pilot RCT comparing SAFE plus TAU with TAU only was successfully completed. As planned, it provided estimates of key parameters, including recruitment and retention, and allows an informed decision regarding the feasibility and optimal design of a definitive trial of SAFE to be made. In this chapter we discuss the estimates, their relation to the two progression criteria established at project outset and the implications.

Positives for feasibility of a definitive trial

The pilot demonstrated that it is possible to identify, consent, randomise and largely retain people from the target population and their SOs in a RCT. This was not a given at the outset because, to our knowledge, no previous trial had focused recruitment on this population and because this population is potentially vulnerable.

No safety concerns arose from the trial's conduct and no protocol deviations occurred. Strategies in the trial to conceal treatment allocation worked. It was possible to get most (76.9%) patient participants who were randomised to the SAFE plus TAU arm to a SAFE session and for it to be delivered as intended (i.e. with high fidelity). This is in line with previous RCTs of complex interventions with the epilepsy population.[71,72,203–205]

Feedback from participants indicated that they valued SAFE and the perceived benefits from receiving it. The SAFE intervention was perceived as being outside current epilepsy service provision. Most said that they would participate in such a trial again if invited.

Importantly, by using routine outcome data on ED use as the basis for the proposed primary outcome measure, it was possible to secure 12-month outcome data for 94% of the randomised patient participants. This means that the second progression criterion – that 12-month follow-up data could be obtained for at least 75% of patient participants – was satisfied. The direct cost for these data was ≈ £10,000. The progression criterion would not have been met had the trial relied on patients self-reporting on ED use because only 67.7% of participants were available and/or able to provide this information. Routine data would thus make a definitive trial less vulnerable to the effect of attrition. By way of context, the proportion of randomised patient participants with primary outcome data in recent NIHR Health Technology Assessment programme trials (conducted between 2005 and 2017) was 89% (IQR 79–97%), but these typically had shorter follow-up periods (median 6 months post randomisation).[131]

Our pilot also revealed that relying on self-reported data would expose a definitive trial to what appears to be recall bias by patients relating to their use of ED. At baseline, 76.2% of patients reported more ED visits during the 12 months prior to recruitment than indicated by routine data for them (on average by 3.8 visits). It has often been claimed that recall bias is not such an issue for 'big ticket' items such as hospitalisations as it is for more routine lower-cost service items (e.g. ambulatory outpatient clinic visits).[206,207] Our findings indicate that caution should be exercised in using self-reported data on ED use.

The proportion of patients who self-reported a different number of ED visits to that recorded by HES was slightly smaller at 12-month follow-up (i.e. 29.4% reported more visits and 38.2% reported fewer). The reason for the greater congruence between the two data sources at this assessment point is not clear. The provision to patient participants at recruitment of seizure diaries by the trial team in which they were encouraged to record seizures and associated events might have attenuated bias.

The apparent bias and the smaller proportion of patients with self-reported ED outcome data meant that the effect size estimate for SAFE differed substantially depending on whether the calculation used self-reported or HES data. When looking at the unadjusted NBR models, the self-reported data indicate that the estimated rate of ED use in the SAFE plus TAU arm was 58% lower than for the TAU arm. HES data indicate that the rate of ED use was around 46% lower.

A microcosting exercise indicated that the cost per attendee (when excluding facilitator travel costs) of attending a SAFE course was ≈ £152. Accurately identifying the cost of an intervention's delivery allows excess treatment costs for a definitive trial to be forecast and helps with assessments regarding the potential for an intervention to be offered in clinical practice. The figure also allows for a simple and preliminary evaluation to be made of the potential for savings to be generated by comparing the cost of the intervention to the direct cost of the health service contact that the intervention seeks to reduce. The average cost of an ED attendance for a suspected seizure in 2007–13 was £123, with an additional £1651 being incurred if the visit resulted in hospital admission (which it did in around half of cases).[34]

Microcosting of complex interventions remains rare. However, it is helpful to note that the NIHR-funded Self-Management education for adults with poorly controlled epILEpsy (SMILE) UK trial did include a microcosting of a self-management education for adults with poorly controlled epilepsy,[208] where the 2014/15 price was estimated to be £56.05 per session. However, the SMILE intervention required multiple sessions, bringing the mean cost associated with the intervention to £180 (inflated to 2017/18 prices). By contrast, the SAFE intervention requires a single session at a comparable cost to the SMILE intervention (between £152 and £194 per delegate). The SAFE cost could be reduced if course attendance could be maximised to the intended level of ≈ 10 patient–SO dyads per course.

Negatives for feasibility of a definitive trial

The pilot revealed that only a small proportion of patients attending ED for a suspected seizure were eligible (10.6%) and willing (12.5%) to participate in a trial. A key reason for ineligibility was intellectual impairment. The leading reason for not wanting to take part was lack of interest. The low rate of uptake means that the other progression criterion stated at the project's outset – that at least 20% of eligible patients agree to participate – was not satisfied.

Low participant uptake does not preclude a definitive trial from happening. It also may not reflect the acceptability of the intervention outside the trial context. In the RCT of the self-management intervention Dose Adjustment for Normal Eating for Type 1 diabetes, which is now offered by the NHS as part of usual care, only 17% of those eligible participated.[97] If the low recruitment rate seen in our pilot trial did reflect patient support or interest in the intervention outside a trial context, this would pose challenges to the intervention's delivery and commission within the NHS since, on average, a single ED was generating only one eligible patient who was willing to take part for every month of attendances.

One reason we set the consent rate criterion was that, with such low participation, there is an increased likelihood that those who do and do not agree to take part may differ in important ways, thus limiting the generalisability of the trial's findings. We compared eligible patients who did and did not agree to take part in the pilot RCT by age, sex and deprivation status. We found no obvious differences in age or deprivation. Females were slightly over-represented. The reason for this is not known (trials generally tend to under-represent females). When telephoning patients about participation in the pilot trial we intentionally attempted telephone calls at different times of the day to minimise the influence of work status on participation.

We do not know if differences existed between participants and non-participants on other indices because access to the wider medical records of non-participants was not ethically permissible. One indication that the pilot trial might not have been recruiting a representative sample was that a high proportion (75.5%) of the recruited patient participants reported having seen an epilepsy specialist within the 12 months prior to the ED attendance that led to their identification. National audit data[28] indicate that most (≈ 65%) PWE attending ED have not done this.

The low uptake seen in the pilot RCT has implication for the likely cost of a definitive trial. In *Chapter 6* we calculated that the sample size required for a definitive trial could be ≈ 680 PWE. This was informed by the pilot trial estimate that SAFE may have only a modest effect on participants' subsequent ED use, reducing it on average by 0.3 ED visits over 12 months (compared with an increase of 0.4 ED visits for the TAU only arm). Based on the participant uptake rate seen in the pilot, 39 recruitment sites could be needed to secure the required sample. The mean cost of NIHR-funded (Health Technology Assessment programme) RCT trials is ≈ £1.3M.[209] The median number of recruitment sites in these trials was only 15.[131] In requiring 2.5 times more sites, a definitive trial of SAFE would be more expensive. This, and the potential unrepresentativeness of the sample likely to take part, could mean that a definitive RCT of SAFE would not represent value for money from a funder's perspective.

It might not even be possible for a definitive trial to secure 39 EDs as recruitment sites. The requirement for them to release clinical personnel to the extent required in the pilot RCT to complete the screening work would not seem realistic considering how stretched most EDs already are in meeting their clinical priorities (e.g. Hassan *et al.*[210]). Thirty-nine EDs equates to about half of type 1 EDs in England. A recent survey[210] highlighted that 62% of ED consultants in the UK viewed their current job as unsustainable and 94% regularly worked in excess of their planned activities.

A final negative to emerge from the pilot trial was that securing the routine outcome data on ED use was not straightforward. For data applications, such as ours, that involve identifiable data and require linkage across a series of data sets, NHS Digital's Service Level Agreements state that these should be processed within ≈ 2 months.[211] In practice, for our pilot RCT it was not until 9 months after the last

participant follow-up assessment at 12 months had been completed that the raw outcome data were secured. This is despite our research team having communicated with the data provider before and during the pilot trial to ensure recruitment and consent approaches were consistent with their requirements. Substantial time from the research team was also required following application submission to respond to queries from the data provider. In addition, despite the current project being funded on the basis of external scientific reviews and its potential significance, the research team in one instance needed to appeal against a decision by the data provider midway through the application process to reject our data request, primarily because of unfounded concerns regarding the project's scientific merit.

Possible modifications to address negatives for progression to definitive trial

Participant uptake

Recruitment of people with uncontrolled epilepsy into evaluative studies has previously been reported to be challenging. In the SMILE (UK) trial,[208] PWE living in the London area who had experienced at least two seizures in the prior year were invited to a trial of self-management that had a 12-month follow-up period;[212] 37% of those invited took part. In a non-randomised trial of self-management for PWE who had attended ED on one or more occasions in the prior 12 months, the uptake rate was 26%.[128] Challenges can arise owing to the nature of the condition itself (e.g. unpredictable but frequent seizures) and its consequences (e.g. anxiety about travelling alone, inability to drive, memory impairment). A range of evidenced-based strategies were therefore used in the pilot RCT to try to maximise recruitment. These included participant vouchers, first-class postage for invitations, flexibility regarding when and where research appointments took place, the use of an 'opt-out' approach to contacting patients about the study, multiple contact attempts and all patient-facing documents being developed collaboratively with a patient and public involvement group. Despite this, a low recruitment rate was experienced.

The characteristics of the recruited patients offers one potential suggestion for the particularly low participant rate seen in the pilot RCT. Specifically, 82% of participants felt stigmatised by their epilepsy, 21.6% highly stigmatised. This is higher than among those with epilepsy generally, including those with uncontrolled seizures (63%).[212] Epilepsy, for reasons rooted deep in its history, has been called a 'stigmatising condition par excellence,'[213] and negative beliefs and lack of knowledge about the condition continue to be present. Consequently, PWE can feel ashamed of their diagnosis, guilty and reluctant to talk about it.[214] Those attending ED appear to be particularly at risk of this. This could be a barrier to participating in research. It is currently unclear how recruitment could be altered to mitigate the feeling of stigmatisation.

It is also worth considering what changes might be possible to who approaches patients regarding participation. Local ED clinicians invited PWE to participate in the pilot RCT. In trials it is usually preferable for a usual care provider with whom a patient has an established relationship to do the inviting. This was not considered ideal for the pilot RCT because national data indicated that most from the target population do not have a specialist usual care provider for their epilepsy (at least not one they have seen recently). Moreover, it was apparent that GPs were often not informed of ED visits made by PWE on their practice registers. Therefore, neither specialists nor GPs are positioned to reliably identify PWE for invite. Given the low participant uptake rate, a modification that a definitive trial could consider making would be for the EDs to identify ostensibly eligible patients from their records and then request that the identified patients' GPs do the inviting. What impact this would have on uptake is not clear. It would require additional NHS support costs and additional approvals to permit EDs to communicate with general practices on what would be a research matter.

One of the leading reasons that patients gave for not wanting to take part was lack of interest. Some of this lack of interest might have arisen because of the time that had elapsed between the ED visit that led to their identification and them receiving the study invite (the median was 9 months). This could be addressed by shortening the time period between identification and invite, or, even more drastically, recruiting patients prospectively instead. The latter would have significant implications for

the resources required by a definitive trial. In addition, the pragmatics of recruiting PWE directly from the ED requires clarification. For example, patients may often be in a post-ictal state and, furthermore, a stay in the ED is typically far shorter than a stay on a hospital ward.

We note that it is possible that the serial assessment of participants and the need for them to complete multiple secondary outcome questionnaires at the assessments might have been seen as overly burdensome by people considering the invitation to participate in the trial. It might also have negatively affected retention of the participants who were recruited. If a definitive trial committed itself to using routine ED data as the source of data for the primary outcome measure, that trial could theoretically reduce or even totally drop the use of the secondary assessment measures. This might increase uptake and improve retention. In considering how dramatic the improvements might be, it is perhaps worth noting that none of the participants who did take part in the trial and who completed the trial participation feedback questionnaire identified the questionnaire packs as being burdensome or as an area of the trial that required improvement.

Identifying eligible patients

Identifying eligible patients for the pilot RCT from ED attendance systems required substantial time and effort on behalf of the local principal investigators at the EDs. This was because of the nature of the condition, because the ED administrative systems did not code visits in a sufficiently granular way and because many of the data on patients that was needed to determine eligibility (e.g. presence of certain comorbidities) was recorded in an unstandardised way in non-searchable, free-text fields. Consequently, searches of the attendances systems were limited to simply identifying persons who had attended for a 'suspected seizure'. The triage cards of these identified persons needed to be accessed and screened by local clinicians to find people suitable for invitation. This activity could not have been delegated to research staff, including research nurses, since it is not ethically permissible for a person outside the patient's care team to access information on their medical history for the purposes of research without prior consent.[215]

Since our pilot RCT took place, a new coding system for EDs – the Emergency Care Data Set[216] – has been phased in. From the perspective of a definitive trial, it brings some advantages because it seeks to standardise and increase the granularity with which presentations and comorbidities are recorded. For example, a specific presentation code for seizure caused by a neurological condition now exists.[216] The system also asks for diagnosis to be recorded using detailed Systematised Nomenclature of Medicine (SNOMED) clinical terms; however, the fields 'discharge diagnosis' and 'comorbidity' in the Emergency Care Data Set are not mandatory.[217,218] Therefore, it remains to be seen how well completed these fields are before it is possible to conclude that the presence of the new system means that PWE can be more readily identified for a definitive trial, and demands on local sites reduced to a reasonable level.

Securing routine outcome data on emergency department use

For a definitive trial of SAFE to be well positioned to be funded and for it to be designed optimally, stakeholders would want to be confident that primary outcome data could be secured and a fairly precise estimate would be needed as to when the data would be available. Our pilot demonstrated that the provision of such data is not a given and that the timeline is hard to estimate. Bodies such as the NIHR have endorsed the use of routine data sources in clinical research. It is possible that, as routine data are requested more often for trials, NHS Digital's application processes will be revised and become more suitable for the research environment. It is notable that our experience is not unique. The challenges in securing routine outcome data from NHS Digital were described in detail by Powell *et al.*[174] in 2017, and recommendations for improvements with the system were made.

Effect of the SAFE intervention

Efficacy was not the primary focus of our pilot RCT. No power calculation was completed and, with such a small sample, imbalance in pre-randomisation covariates between the treatment arms is possible. The estimated modest effect of SAFE on subsequent ED use – namely, reducing it from

2.1 visits over a 12-month period to 1.8 (compared with a slight increase in the TAU only arm from 3.0 to 3.4 visits) – was used to inform the sample size calculations for a definitive trial. Therefore, it is important to consider how realistic this estimate is because a larger effect would probably make a definitive trial cheaper (i.e. because fewer patient participants and thus recruitment sites would be required).

When the pilot RCT was being designed the empirical evidence on the ability of self-management interventions to change behaviour in PWE was positive but inconclusive. An updated systematic review by Luedke *et al.*[219] has since been published. It considered evidence from 13 randomised trials and two non-randomised trials of self-management interventions for epilepsy published before April 2018. The review concluded that interventions showed clinically important benefit on only a limited number of outcome measures. Interventions that primarily sought to increase knowledge changed self-management behaviours moderately, whereas interventions that included techniques such as cognitive behavioural therapy or problem-solving treatment improved quality of life only modestly. Overall, self-management interventions were not found to decrease seizure rates.

One RCT from the USA[220] identified by Luedke *et al.*'s review[219] is particularly instructive because it is the only one to have also considered change in ED use. It focused on what its authors, Sajatovic *et al.*,[220] labelled an 'at-risk' population, defined as adults with established epilepsy who had had at least one negative health event within the past 6 months, be it a seizure, an accident, a self-harm attempt or an ED visit. The RCT compared the effects of an educational intervention, called 'self-management for people with epilepsy and a history of negative health events', to a wait list control. It comprised eight sessions, addressed myths surrounding epilepsy and introduced participants to key self-management tasks. A total of 120 patients were recruited and followed up for 6 months. The trial found no statistically significant differences between arms in terms of subsequent ED/hospitalisation use. For the intervention arm it reduced by 0.44 visits from 1.22 visits. For the wait list control arm it reduced by −1.26 visits from 2.4 visits.

The findings of the updated review suggest that the relatively small estimated effect of SAFE is in the region of what might be expected of a self-management intervention and thus the estimate from our pilot trial constitutes a reasonable basis for the sample size calculations for a definitive trial. That a self-management intervention reduces ED visits by a only small amount also makes sense from a clinical perspective because we now know that factors beyond low seizure confidence can influence whether or not an ED visit occurs. One is that studies with the ambulance service show that peripheral issues, such as performance targets and difficulties accessing information on patient medical history to determine normality or otherwise of the seizure presentation, can influence whether or not a person is conveyed to ED following an emergency call.[77,78]

Progression, feasibility and optimal design of a definitive trial

Thabane *et al.*[132] provide a framework for judging whether or not to proceed to a definitive trial following a pilot. They describe the options as (1) 'continue without modification' (feasible as it is), (2) 'continue without modifications, but monitor closely' (feasible with close monitoring), (3) 'continue, but modify the protocol' (feasible with modifications) and (4) 'stop' (main study is not feasible). In satisfying only one of the pre-specified progression criteria, a definitive trial based on our pilot trial's design is not feasible. On the basis of the discussion above, we do not consider that any options are currently available to modify the protocol in such a way for it to become feasible. Therefore, we recommend not proceeding to a definitive trial.

Alternative steps to the diffusion of the SAFE intervention

A definitive trial of SAFE is needed to determine its efficacy. This information would help commissioners understand with confidence whether or not SAFE should be scaled up and rolled out. As noted, our pilot indicates that such a trial is not currently feasible, although it might be in the future. In the meantime,

the needs of many PWE who visit ED with respect to seizure first aid will continue to be unmet, with all the consequences that this has. Because it is not known when any other intervention will become available, an argument can be made for making SAFE available in some form to the epilepsy population now.

In support of this approach is that SAFE was rigorously produced, including the key information that health-care professional representatives reported that the target population needs to routinely receive (but for various reasons often do not). It received positive support from service users, with most who received it welcoming it. There were also no indications that SAFE had any serious adverse effects and it might reduce some ED use.

One way of making SAFE available now would be to convert its materials into a free online resource to which health-care professionals, such as epilepsy nurses and neurologists, and charities could direct interested people. The conversion could be in the form of a professionally produced video of a SAFE course that could be run with agreeable service users. To engage those viewing the online resource, interactive questions could be integrated into recordings.

The conversion would be a relatively straightforward process and allow the investment already made via this project to be capitalised on. To enable the conversion, only modest funding would be required to produce the website and maintain and update it over time. For the pilot RCT, a more basic website was developed for trial participants to allow them to download (rather than interact with) the course slides and videos of the recovery position. The costs of the former activity provide some guidance as to the sort of costs required. In 2017–18 the website domain cost the project £20.94 for 5 years and the hourly rate for an information technology (IT) technician to maintain the site was only £28.09.

It is likely that a full conversion of SAFE would be welcomed by many health-care professionals because specialist services are currently being asked to innovate, identify and care for those currently underserved, such as PWE who visit EDs. However, the workforce is small and can already struggle to achieve waiting time targets and respond to requests for help.

Sharing SAFE in the way described would also present new opportunities to evaluate SAFE's effect with a potentially large sample over time, albeit in a less rigorous way than by a full RCT. For instance, by using a pre–post design, those viewing the materials could be asked to fill in a brief online questionnaire immediately before and after the intervention to provide a measure of the intervention's effect on seizure first aid knowledge and confidence. The same people could be asked for consent for access to be given to routine data from NHS Digital on its use of ED during the 12 months before and after completion of the course.

Strengths and limitations

Intervention development

The intervention was co-produced. The process enabled us to access the unique perspectives of health-care professionals and service users in a non-tokenistic way. Clear, tangible changes to the intervention were made in response to their views. The APEASE framework[116] provides criteria that need to be considered when considering the utility and potential of interventions. Our project has provided positive evidence for the SAFE intervention on a number of these criteria, namely acceptability, practicability, affordability and safety. SAFE is well positioned to be implemented in the NHS should this ultimately prove appropriate.

We anticipate that the description provided of the co-production process we adopted could also provide a useful template for the development of interventions by other groups. A concern of some researchers is that the process of engaging service users and other stakeholders will be unwieldy and it will be challenging to engage stakeholders.[221] To this point we note that this process is not one that should be

entered into lightly because it requires careful planning, expertise, resources and ethics approval. It took 9 months to complete, with a team including four experienced academics, two at the professorial level. However, we would argue that the length of the feedback sessions and the quality of consideration given by the stakeholders goes some way to demonstrating how willing stakeholders can be to contribute to such processes. In terms of recruitment, we note that those with epilepsy can often have low self-esteem and confidence.[186,213] This meant that we needed to be mindful from the start of the need, when bringing people into this process, to clearly emphasise to participants what we were doing, why we wanted them involved and that it was their views, however critical, that we needed to hear.

Pilot trial

The pilot trial was completed in a rigorous manner in accordance with best practice guidelines and reported according to the CONSORT extension for randomised pilot and feasibility trial[222] (see *Report Supplementary Material 3*). Randomisation was done remotely by computer and stratification factors and allocations concealed from those collecting baseline and follow-up data and analysing them. Patients were also recruited from NHS sites. Some RCTs, including Sajatovic *et al.*'s trial,[220] have focused recruitment on user group participants. People in such groups might differ in important ways from those who are not. We also used an opt-out method of recruitment whereby we contacted patients about the study unless they told us otherwise. The opt-in method, where the onus is on the patient to contact the research team to express their interest, was not considered ideal for a patient population that frequently reports memory problems and whose lives can be disrupted by episodic relapses of their condition. Another strength is that recruitment sites were in areas where social deprivation was high and epilepsy control poor and so similar to those where a definitive trial would probably need to focus recruitment.

We completed one of the few microcostings of a self-management intervention for epilepsy. We also described the content of the SAFE intervention in detail and independently monitored its fidelity and reported the results. A recent review of trials of psychosocial interventions for epilepsy found that only ≈ 5% of trials did this for 'adherence' and ≈ 2% for 'competence'.[223] Indeed, we have also provided a rare worked example of how to conduct a fidelity assessment and the resources required. Medical Research Council publications[224] note the importance of evaluating fidelity; however, minimal guidance is provided regarding how to do it. Intervention developers report that this is one reason why they fail to assess fidelity.[225]

The pilot trial is not without potential weaknesses. First, despite the trial team identifying PWE for inclusion on the basis of them having at least one attendance at ED for epilepsy recorded and the patient, when questioned, reporting at least two visits in the 12 months prior to recruitment, ≈ 40% of these patients might not have met the inclusion criteria (according to the routine health data subsequently obtained). The inclusion of these people could affect the external validity of the trial and attenuate the estimated effect of SAFE because they had less opportunity for a reduction in ED use.

In addition, while 18 (69%) of the 26 patient participants randomised to SAFE took part with an informal carer, five (28%) of these did not ultimately attend an intervention session. This is comparable to experience in the SMILE (UK) trial.[208] Their non-attendance may have limited the effect of SAFE because carers can be key to decision-making when a seizure occurs.

Because a diagnostic code is often not recorded for ED visits, we asked NHS Digital to inform us how many ED visits, regardless of diagnosis, each patient had made during specific periods of time. Therefore, it is possible that not all of the visits reported for the participants were associated with epilepsy. UK data on how many ED visits a person with epilepsy has made for reasons other than epilepsy in a set period is not known. PWE are certainly more likely to have a comorbidity than the general population and so it is possible that they attend for other reasons.

When calculating the size of sample probably required for a definitive trial of SAFE, the pilot trial's estimate of SAFE's effect on ED use was used. We used the estimate because there is no consensus

about what constitutes a minimally important clinical reduction in ED visits. We acknowledge that the estimate from the pilot trial might be lacking in precision[133] and that basing the sample size calculations on a smaller or larger effect size would substantially change the required sample size for a definitive trial.

Implications for NHS service commissioning, policy and practice

- The trial was not designed to determine SAFE's efficacy. There remains limited evidence to justify the commissioning of such a service.
- Some PWE are unknown to ambulatory care services and cannot be readily identified. Increasing the granularity with which attendances at EDs are coded could enable them to be readily identified, supported and involved in research.
- Using routine data on ED could make trials less vulnerable to losses to follow-up and mean that they are not exposed to apparent recall bias. Stakeholders need to be given more assurances from those holding the data that it is likely to be provided and done so in a timely manner.
- Given that SAFE is liked by service users, that it might reduce ED use in a small way and that it does not appear to have serious adverse effects, there is a case for converting it into an free online resource that people could be directed to in the short term to go some way to address the otherwise unmet seizure first aid training needs of PWE who visit EDs and their SOs.

Recommendations for research

- A definitive SAFE trial, with its current design, should not be conducted because it is not feasible for the reasons given above. We cannot envisage any immediate changes to trial design that could make it feasible.
- Research is required to understand how people from the target population can be better recruited. It is possible that the feelings of stigma apparent in the target population might be an important barrier to recruitment. If this is the case, it is important that recruitment methods are identified or developed to ensure that participants' feelings of stigma do not compound the difficulties that they may already be facing by preventing high-quality research into their condition from being conducted.
- Converting SAFE into a free online resource that people could be directed to could provide an opportunity for an alternative method of evaluating its effect on some of the primary and secondary outcome measures used in the pilot RCT. Via a pre–post design, people accessing the online resource could complete brief measures to assess change in seizure first aid confidence and skills. They could also be asked for consent to access routine data on their use of EDs in the 12 months before and after their viewing of the resource.

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Contributions of authors

Adam Noble (https://orcid.org/0000-0002-8070-4352) (Senior Lecturer in Health Services Research) was chief investigator and led in the conception and design of the study, the supervision and co-ordination of the study, the interpretation of the data and, with Darlene Snape and Sarah Nevitt, the writing of the final report.

Sarah Nevitt (https://orcid.org/0000-0001-9988-2709) (Research Associate, Biostatistics) contributed to conducting the study, developed and conducted the statistical analysis of the quantitative data and helped write the final report.

Emily Holmes (https://orcid.org/0000-0002-0479-5336) (Research Fellow, Pharmacoeconomics) contributed to the design of the study, developed and conducted the statistical analysis of the health economic data and wrote up the health economics results for the final report.

Leone Ridsdale (https://orcid.org/0000-0002-2234-2859) (Professor of Neurology and General Practice) supported Adam Noble in the conception and design of the study, contributed to its conduct and reviewed the final report.

Myfanwy Morgan (https://orcid.org/0000-0001-5532-8941) (Professor of Medical Sociology) contributed to the design of study and its conduct, oversaw its qualitative aspects and reviewed the final report.

Catrin Tudur-Smith (https://orcid.org/0000-0003-3051-1445) (Professor in Medical Statistics) contributed to the design of study, supervised the statistical analysis of the quantitative data and reviewed the report.

Dyfrig Hughes (https://orcid.org/0000-0001-8247-7459) (Professor in Pharmacoeconomics) contributed to the design of the study, supervised the collection of health economic data and its analysis and reviewed the final report.

Steve Goodacre (https://orcid.org/0000-0003-0803-8444) (Professor of Emergency Medicine) contributed to the design of the research and its conduct and reviewed the final report.

Tony Marson (https://orcid.org/0000-0002-6861-8806) (Professor of Neurology) contributed to the design of the research and its conduct and reviewed the final report.

Darlene Snape (https://orcid.org/0000-0002-0787-3299) (Research Fellow, Health Services Research) was responsible for setting up the study, for participant recruitment and assessment and for analysis and interpretation of the qualitative findings and helped write the final report.

Publications

Noble AJ, Marson AG, Tudur-Smith C, Morgan M, Hughes DA, Goodacre S, *et al.* 'Seizure First Aid Training' for people with epilepsy who attend emergency departments, and their family and friends: study protocol for intervention development and a pilot randomised controlled trial. *BMJ Open* 2015;**5**:e009040.

Noble AJ, Snape D, Morgan M, Goodacre S, Marson A, Ridsdale L. Seizure first aid training for people with epilepsy attending emergency departments, and SOs. *J Neurol Neurosurg Psychiat* 2017;**88**:A25.

Snape DA, Morgan M, Ridsdale L, Goodacre S, Marson AG, Noble AJ. Developing and assessing the acceptability of an epilepsy first aid training intervention for patients who visit UK emergency departments: a multi-method study of patients and professionals. *Epilepsy Behav* 2017;**68**:177–85.

Snape D, Nevitt S, Tudur-Smith C, Goodacre S, Hughes DA, Morgan M, *et al.* Seizure first aid training for people with epilepsy who attend emergency departments and their family and friends: results from a pilot randomised controlled trial. *Epilepsia* 2018;**59**:S140.

Noble A, Snape D, Ridsdale L, Morgan M, Nevitt SJ, Goodacre S, Marson A. Assessing treatment fidelity within an epilepsy randomized controlled trial – seizure first aid training for people with epilepsy who visit emergency departments. *Behav Neurol* 2019;**3**:5048794.

Noble AJ, Snape D, Nevitt S, Holmes EAF, Morgan M, Tudur Smith C, *et al.* Seizure First Aid Training For people with Epilepsy (SAFE) frequently attending emergency departments and their significant others: results of a UK multi-centre randomised controlled pilot trial. *BMJ Open* 2020;**10**:e035516.

Presentations

Snape D, Morgan M, Ridsdale L, Goodacre S, Marson AG, Noble AJ. *Developing and Assessing Acceptability of Seizure First-Aid Training for Emergency Department Users with Epilepsy*. Presented at the Association of British Neurologists Conference, Liverpool, 3–5 May 2017.

Snape D, Nevitt S, Tudur-Smith C, Goodacre S, Hughes DA, Morgan M, *et al. Seizure First Aid Training for People with Epilepsy who Attend Emergency Departments and their Family and Friends: Results from a Pilot Randomised Controlled Trial*. Presented at the 13th European Conference on Epileptology, Vienna, 26–30 August 2018.

Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Patient data

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety, and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that it is stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation.

References

1. Longmore M, Wilkinson I, Baldwin A, Wallin E. *Oxford Handbook of Clinical Medicine*. 9th edn. Oxford: Oxford University Press; 2014. https://doi.org/10.1093/med/9780199609628.001.0001
2. Smithson WH, Walker MC. *ABC of Epilepsy*. 1st edn. Chichester: Wiley-Blackwell; 2012.
3. Ridsdale L, Charlton J, Ashworth M, Richardson MP, Gulliford MC. Epilepsy mortality and risk factors for death in epilepsy: a population-based study. *Br J Gen Pract* 2011;**61**:e271–8. https://doi.org/10.3399/bjgp11X572463
4. MacDonald BK, Cockerell OC, Sander JW, Shorvon SD. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. *Brain* 2000;**123**:665–76. https://doi.org/10.1093/brain/123.4.665
5. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, *et al.* ILAE official report: a practical clinical definition of epilepsy. *Epilepsia* 2014;**55**:475–82. https://doi.org/10.1111/epi.12550
6. Forsgren L, Beghi E, Oun A, Sillanpää M. The epidemiology of epilepsy in Europe – a systematic review. *Eur J Neurol* 2005;**12**:245–53. https://doi.org/10.1111/j.1468-1331.2004.00992.x
7. Aidan NGS, Bell GS, Johnson AL, Goodridge DM, Shorvon SD, Sander JW. The long-term risk of premature mortality in people with epilepsy. *Brain* 2011;**134**:388–95. https://doi.org/10.1093/brain/awq378
8. Ridsdale L. Avoiding premature death in epilepsy. *BMJ* 2015;**350**:h718. https://doi.org/10.1136/bmj.h718
9. Moran NF, Poole K, Bell G, Solomon J, Kendall S, McCarthy M, *et al.* Epilepsy in the United Kingdom: seizure frequency and severity, anti-epileptic drug utilization and impact on life in 1652 people with epilepsy. *Seizure* 2004;**13**:425–33. https://doi.org/10.1016/j.seizure.2003.10.002
10. Fisher RS, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, Engel J. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* 2005;**46**:470–2. https://doi.org/10.1111/j.0013-9580.2005.66104.x
11. Räty LK, Wilde-Larsson BM. Patients' perceptions of living with epilepsy: a phenomenographic study. *J Clin Nurs* 2011;**20**:1993–2002. https://doi.org/10.1111/j.1365-2702.2010.03572.x
12. Jacoby A, Snape D, Baker GA. Epilepsy and social identity: the stigma of a chronic neurological disorder. *Lancet Neurol* 2005;**4**:171–8. https://doi.org/10.1016/S1474-4422(05)70020-X
13. McLaughlin DP, Pachana NA, Mcfarland K. Stigma, seizure frequency and quality of life: the impact of epilepsy in late adulthood. *Seizure* 2008;**17**:281–7. https://doi.org/10.1016/j.seizure.2007.09.001
14. Taylor J, Baker GA, Jacoby A. Levels of epilepsy stigma in an incident population and associated factors. *Epilepsy Behav* 2011;**21**:255–60. https://doi.org/10.1016/j.yebeh.2011.04.002
15. Pugliatti M, Beghi E, Forsgren L, Ekman M, Sobocki P. Estimating the cost of epilepsy in Europe: a review with economic modeling. *Epilepsia* 2007;**48**:2224–33. https://doi.org/10.1111/j.1528-1167.2007.01251.x
16. Kitson A, Shorvon S. Clinical Standards Advisory Group. *Services for Patients with Epilepsy: A Report of a CSAG Committee*. London: Department of Health and Social Care; 2000.

17. Jacoby A, Buck D, Baker G, McNamee P, Graham-Jones S, Chadwick D. Uptake and costs of care for epilepsy: findings from a U.K. regional study. *Epilepsia* 1998;**39**:776–86. https://doi.org/10.1111/j.1528-1157.1998.tb01164.x

18. Hart YM, Shorvon SD. The nature of epilepsy in the general population. II. Medical care. *Epilepsy Res* 1995;**21**:51–8. https://doi.org/10.1016/0920-1211(95)00008-X

19. Ryan J, Nash S, Lyndon J. Epilepsy in the accident and emergency department – developing a code of safe practice for adult patients. South East and South West Thames Accident and Emergency Specialty Sub-committees. *J Accid Emerg Med* 1998;**15**:237–43. https://doi.org/10.1136/emj.15.4.237

20. Pearson M, Marson T, Dixon P, Scott K. *National Audit of Seizure Management in Hospitals: St. Elsewhere's Hospital – Clinical Report: April 2014*. 2014. URL: www.nashstudy.org.uk/Newsletters/St%20Elsewhere%27s%20Clinical%20Report%20NASH%202.pdf (accessed 24 April 2018).

21. Pearson M, Marson T, Dixon P, Billington K. *National Audit of Seizure Management in Hospitals: St. Elsewhere's Hospital – Clinical Report: April 2012*. 2012. URL: www.nashstudy.org.uk/Newsletters/St%20Elsewhere%27s%20NASH%20Report.pdf (accessed 24 April 2018).

22. House of Commons Committee of Public Accounts. *Services to People with Neurological Conditions: Progress Review*. London: House of Commons; 2016. URL: https://publications.parliament.uk/pa/cm201516/cmselect/cmpubacc/502/502.pdf (accessed 24 April 2018).

23. Reuber M, Hattingh L, Goulding PJ. Epileptological emergencies in accident and emergency: a survey at St James's university hospital, Leeds. *Seizure* 2000;**9**:216–20. https://doi.org/10.1053/seiz.2000.0386

24. Bruce M, Griffiths C, Brock A, Majeed A. Trends in mortality and hospital admissions associated with epilepsy in England and Wales during the 1990s. *Health Stat Q* 2004;**21**:23–9.

25. Bardsley M, Blunt I, Davies S, Dixon J. Is secondary preventive care improving? Observational study of 10-year trends in emergency admissions for conditions amenable to ambulatory care. *BMJ Open* 2013;**3**:e002007. https://doi.org/10.1136/bmjopen-2012-002007

26. NHS Digital. *CCG Outcomes Indicator Set – June 2013: Emergency Admissions*. Leeds: NHS Digital; 2013. URL: https://digital.nhs.uk/data-and-information/publications/statistical/ccg-outcomes-indicator-set/june-2013/ccg-outcomes-indicator-set—june-2013 (accessed 4 August 2017).

27. Noble AJ, Goldstein LH, Seed P, Glucksman E, Ridsdale L. Characteristics of people with epilepsy who attend emergency departments: prospective study of metropolitan hospital attendees. *Epilepsia* 2012;**53**:1820–8. https://doi.org/10.1111/j.1528-1167.2012.03586.x

28. Dixon PA, Kirkham JJ, Marson AG, Pearson MG. National Audit of Seizure management in Hospitals (NASH): results of the national audit of adult epilepsy in the UK. *BMJ Open* 2015;**5**:e007325. https://doi.org/10.1136/bmjopen-2014-007325

29. Whiston S, Coyle B, Chappel D. *Health Needs Assessment for Long Term Neurological Conditions in North East England*. Stockton on Tees: North East Public Health Observatory; 2009.

30. Dickson JM, Jacques R, Reuber M, Hick J, Campbell MJ, Morley R, Grünewald RA. Emergency hospital care for adults with suspected seizures in the NHS in England 2007–2013: a cross-sectional study. *BMJ Open* 2018;**8**:e023352. https://doi.org/10.1136/bmjopen-2018-023352

31. Ridsdale L, Virdi C, Noble A, Morgan M. Explanations given by people with epilepsy for using emergency medical services: a qualitative study. *Epilepsy Behav* 2012;**25**:529–33. https://doi.org/10.1016/j.yebeh.2012.09.034

32. Noble AJ, Morgan M, Virdi C, Ridsdale L. A nurse-led self-management intervention for people who attend emergency departments with epilepsy: the patients' view. *J Neurol* 2013;**260**:1022–30. https://doi.org/10.1007/s00415-012-6749-2

33. Moore L, Deehan A, Seed P, Jones R. Characteristics of frequent attenders in an emergency department: analysis of 1-year attendance data. *Emerg Med J* 2009;**26**:263–7. https://doi.org/10.1136/emj.2008.059428

34. Dickson JM, Taylor LH, Shewan J, Baldwin T, Grünewald RA, Reuber M. Cross-sectional study of the prehospital management of adult patients with a suspected seizure (EPIC1). *BMJ Open* 2016;**6**:e010573. https://doi.org/10.1136/bmjopen-2015-010573

35. Allen L, Jones CT. Emergency department use of computed tomography in children with epilepsy and breakthrough seizure activity. *J Child Neurol* 2007;**22**:1099–101. https://doi.org/10.1177/0883073807306249

36. Limm EI, Fang X, Dendle C, Stuart RL, Egerton Warburton D. Half of all peripheral intravenous lines in an Australian tertiary emergency department are unused: pain with no gain? *Ann Emerg Med* 2013;**62**:521–5. https://doi.org/10.1016/j.annemergmed.2013.02.022

37. Peterson CL, Walker C, Coleman H. 'I hate wasting the hospital's time': experiences of emergency department admissions of Australian people with epilepsy. *Epilepsy Behav* 2019;**90**:228–32. https://doi.org/10.1016/j.yebeh.2018.11.018

38. Craig J, Patterson V, Rocke L, Jamison J. Accident and emergency neurology: time for a reappraisal? *Health Trends* 1997;**29**:89–91.

39. O'Cathain A, Knowles E, Turner J, Maheswaran R, Goodacre S, Hirst E, *et al.* Explaining variation in emergency admissions: a mixed-methods study of emergency and urgent care systems. *Health Serv Deliv Res* **2**(48). https://doi.org/10.3310/hsdr02480

40. Bautista RE, Glen ET, Wludyka PS, Shetty NK. Factors associated with utilization of healthcare resources among epilepsy patients. *Epilepsy Res* 2008;**79**:120–9. https://doi.org/10.1016/j.eplepsyres.2008.01.003

41. Public Health England. *The NHS Atlas of Variation in Healthcare: November 2010*. London: Public Health England; 2010. URL: https://fingertips.phe.org.uk/documents/Atlas_2010%20Compendium.pdf (accessed 25 April 2018).

42. Public Health England. *The NHS Atlas of Variation in Healthcare: November 2011*. London: Public Health England; 2011. URL: https://fingertips.phe.org.uk/documents/Atlas_2011%20Compendium.pdf (accessed 25 April 2018).

43. Sajatovic M, Welter E, Tatsuoka C, Perzynski AT, Einstadter D. Electronic medical record analysis of emergency room visits and hospitalizations in individuals with epilepsy and mental illness comorbidity. *Epilepsy Behav* 2015;**50**:55–60. https://doi.org/10.1016/j.yebeh.2015.05.016

44. Public Health England. *The NHS Atlas of Variation in Healthcare: November 2015*. London: Public Health England; 2015. URL: https://fingertips.phe.org.uk/documents/Atlas_2015%20Compendium.pdf (accessed 25 April 2018).

45. Allard J, Shankar R, Henley W, Brown A, McLean B, Jadav M, *et al.* Frequency and factors associated with emergency department attendance for people with epilepsy in a rural UK population. *Epilepsy Behav* 2017;**68**:192–5. https://doi.org/10.1016/j.yebeh.2017.01.017

46. Ashworth M, Seed P, Armstrong D, Durbaba S, Jones R. The relationship between social deprivation and the quality of primary care: a national survey using indicators from the UK Quality and Outcomes Framework. *Br J Gen Pract* 2007;**57**:441–8.

47. Shohet C, Yelloly J, Bingham P, Lyratzopoulos G. The association between the quality of epilepsy management in primary care, general practice population deprivation status and epilepsy-related emergency hospitalisations. *Seizure* 2007;**16**:351–5. https://doi.org/10.1016/j.seizure.2007.02.005

48. Morgan CL, Ahmed Z, Kerr MP. Social deprivation and prevalence of epilepsy and associated health usage. *J Neurol Neurosurg Psychiatry* 2000;**69**:13–17. https://doi.org/10.1136/jnnp.69.1.13

49. National Institute for Health and Care Excellence (NICE). *Epilepsies: Diagnosis and Management. Clinical Guideline [CG137]*. London: NICE; 2012. URL: www.nice.org.uk/guidance/cg137 (accessed 21 August 2019).

50. Grainger R, Pearson M, Dixon P, Devonport E, Timoney M, Bodger K, *et al.* Referral patterns after a seizure admission in an English region: an opportunity for effective intervention? An observational study of routine hospital data. *BMJ Open* 2016;**6**:e010100. https://doi.org/10.1136/bmjopen-2015-010100

51. House of Commons Committee of Public Accounts. *Financial Sustainability of the NHS*. London: House of Commons; 2017. URL: http://publications.parliament.uk/pa/cm201617/cmselect/cmpubacc/887/887.pdf (accessed 24 April 2018).

52. Anandaciva S. *Nine Things We Learnt About Provider Finances in 2016/17*. 2017. URL: www.kingsfund.org.uk/publications/nine-things-NHS-provider-finances-2016-17 (accessed 24 April 2018).

53. Department of Health and Social Care (DHSC). *The NHS Plan: A Plan for Investment, a Plan for Reform*. London: DHSC; 2000.

54. NHS England. *Five Year Forward View*. 2014. URL: www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf (accessed 8 August 2017).

55. NHS England. *Next Step on the NHS Five Year Forward View*. 2017. URL: www.england.nhs.uk/wp-content/uploads/2017/03/next-steps-on-the-nhs-five-year-forward-view.pdf (accessed 8 August 2017).

56. NHS Digital. *NHS Outcomes Framework indicators – February 2017 Release*. Leeds: NHS Digital; 2017. URL: https://digital.nhs.uk/data-and-information/publications/statistical/nhs-outcomes-framework/february-2017/nhs-outcomes-framework-indicators—february-2017-release (accessed 8 August 2017).

57. National Institute for Health Research (NIHR). *Glossary*. 2012. URL: www.nihr.ac.uk/glossary (accessed 21 August 2017).

58. Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. *Patient Educ Couns* 2002;**48**:177–87. https://doi.org/10.1016/S0738-3991(02)00032-0

59. Dilorio C, Faherty B, Manteuffel B. The development and testing of an instrument to measure self-efficacy in individuals with epilepsy. *J Neurosci Nurs* 1992;**24**:9–13. https://doi.org/10.1097/01376517-199202000-00004

60. Jarvie S. *Self Perception and Psychosocial Functioning in People with Intractable Epilepsy*. PhD thesis. Glasgow: University of Glasgow; 1993.

61. Wagner AK, Keller SD, Kosinski M, Baker GA, Jacoby A, Hsu MA, *et al.* Advances in methods for assessing the impact of epilepsy and antiepileptic drug therapy on patients' health-related quality of life. *Qual Life Res* 1995;**4**:115–34. https://doi.org/10.1007/BF01833606

62. Jacoby A. Felt versus enacted stigma: a concept revisited. Evidence from a study of people with epilepsy in remission. *Soc Sci Med* 1994;**38**:269–74. https://doi.org/10.1016/0277-9536(94)90396-4

63. Morgan GA, Harmon RJ, Maslin-Cole CA. Mastery motivation: definition and measurement. *Early Edu Dev* 1990;**1**:318–39. https://doi.org/10.1207/s15566935eed0105_1

64. Au A, Chan F, Li K, Leung P, Li P, Chan J. Cognitive-behavioral group treatment program for adults with epilepsy in Hong Kong. *Epilepsy Behav* 2003;**4**:441–6. https://doi.org/10.1016/S1525-5050(03)00149-5

65. Corbin JM, Strauss A. *Unending Work and Care: Managing Chronic Illness at Home*. San Francisco, CA: Jossey-Bass; 1988.

66. Deveugele M, Derese A, van den Brink-Muinen A, Bensing J, De Maeseneer J. Consultation length in general practice: cross sectional study in six European countries. *BMJ* 2002;**325**:472. https://doi.org/10.1136/bmj.325.7362.472

67. Royal College of Physicians (RCP). *Consultant Physicians Working with Patients – Revised 5th Edition*. London: RCP; 2013. URL: www.rcplondon.ac.uk/projects/outputs/consultant-physicians-working-patients-revised-5th-edition (accessed 29 August 2018).

68. Gilliam F, Penovich PE, Eagan CA, Stern JM, Labiner DM, Onofrey M, *et al.* Conversations between community-based neurologists and patients with epilepsy: results of an observational linguistic study. *Epilepsy Behav* 2009;**16**:315–20. https://doi.org/10.1016/j.yebeh.2009.07.039

69. Ridsdale L, Morgan M, O'Connor C. Promoting self-care in epilepsy: the views of patients on the advice they had received from specialists, family doctors and an epilepsy nurse. *Patient Educ Couns* 1999;**37**:43–7. https://doi.org/10.1016/S0738-3991(98)00094-9

70. Long L, Reeves AL, Moore JL, Roach J, Pickering CT. An assessment of epilepsy patients' knowledge of their disorder. *Epilepsia* 2000;**41**:727–31. https://doi.org/10.1111/j.1528-1157.2000.tb00235.x

71. Ridsdale L, Kwan I, Cryer C. The effect of a special nurse on patients' knowledge of epilepsy and their emotional state. Epilepsy Evaluation Care Group. *Br J Gen Pract* 1999;**49**:285–9.

72. Ridsdale L, Kwan I, Cryer C. Newly diagnosed epilepsy: can nurse specialists help? A randomized controlled trial. Epilepsy Care Evaluation Group. *Epilepsia* 2000;**41**:1014–19. https://doi.org/10.1111/j.1528-1157.2000.tb00287.x

73. Walker ER, Bamps Y, Burdett A, Rothkopf J, Diiorio C. Social support for self-management behaviors among people with epilepsy: a content analysis of the WebEase program. *Epilepsy Behav* 2012;**23**:285–90. https://doi.org/10.1016/j.yebeh.2012.01.006

74. Swanborough N. *Not Always A&E*. 2014. URL: www.epilepsysociety.org.uk/not-always-a%26e-07-02-2014#.Xt9Vvi2ZMkg (accessed 27 August 2019).

75. Hunt N, Touquet VL. Known epileptic patients brought to the accident and emergency department. *J R Coll Gen Pract* 1986;**36**:224–5.

76. BBC News. Health: public 'ignorant' about epilepsy. *BBC News*, 10 May 1999. URL: http://news.bbc.co.uk/1/hi/health/339872.stm (accessed 27 August 2019).

77. Noble AJ, Snape D, Goodacre S, Jackson M, Sherratt FC, Pearson M, Marson A. Qualitative study of paramedics' experiences of managing seizures: a national perspective from England. *BMJ Open* 2016;**6**:e014022. https://doi.org/10.1136/bmjopen-2016-014022

78. Burrell L, Noble A, Ridsdale L. Decision-making by ambulance clinicians in London when managing patients with epilepsy: a qualitative study. *Emerg Med J* 2013;**30**:236–40. https://doi.org/10.1136/emermed-2011-200388

79. Ridsdale L. The social causes of inequality in epilepsy and developing a rehabilitation strategy: a UK-based analysis. *Epilepsia* 2009;**50**:2175–9. https://doi.org/10.1111/j.1528-1167.2009.02150.x

80. NHS England. *Patient Activation: People's Ability to Manage their Own Health and Wellbeing*. London: NHS England; 2018.

81. Foster G, Taylor SJ, Eldridge SE, Ramsay J, Griffiths CJ. Self-management education programmes by lay leaders for people with chronic conditions. *Cochrane Database Syst Rev* 2007;**4**:CD005108. https://doi.org/10.1002/14651858.CD005108.pub2

82. Davies MJ, Heller S, Skinner TC, Campbell MJ, Carey ME, Cradock S, *et al.* Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trials. *BMJ* 2008;**336**:491–5. https://doi.org/10.1136/bmj.39474.922025.BE

83. Deakin TA, Cade JE, Williams R, Greenwood DC. Structured patient education: the diabetes X-PERT programme makes a difference. *Diabet Med* 2006;**23**:944–54. https://doi.org/10.1111/j.1464-5491.2006.01906.x

84. Barlow JH, Turner AP, Wright CC. A randomized controlled study of the Arthritis Self-Management Programme in the UK. *Health Educ Res* 2000;**15**:665–80. https://doi.org/10.1093/her/15.6.665

85. Buszewicz M, Rait G, Griffin M, Nazareth I, Patel A, Atkinson A, *et al.* Self management of arthritis in primary care: randomised controlled trial. *BMJ* 2006;**333**:879. https://doi.org/10.1136/bmj.38965.375718.80

86. Willis E. The making of expert patients: the role of online health communities in arthritis self-management. *J Health Psychol* 2014;**19**:1613–25. https://doi.org/10.1177/1359105313496446

87. Tieffenberg JA, Wood EI, Alonso A, Tossutti MS, Vicente MF. A randomized field trial of ACINDES: a child-centered training model for children with chronic illnesses (asthma and epilepsy). *J Urban Health* 2000;**77**:280–97. https://doi.org/10.1007/BF02390539

88. Tapp S, Lasserson TJ, Rowe B. Education interventions for adults who attend the emergency room for acute asthma. *Cochrane Database Syst Rev* 2007;**3**:CD003000. https://doi.org/10.1002/14651858.CD003000.pub2

89. Boyd M, Lasserson TJ, McKean MC, Gibson PG, Ducharme FM, Haby M. Interventions for educating children who are at risk of asthma-related emergency department attendance. *Cochrane Database Syst Rev* 2009;**2**:CD001290. https://doi.org/10.1002/14651858.CD001290.pub2

90. Institute of Medicine. *Priority Areas for National Action: Transforming Health Care Quality*. Washington, DC: National Academies Press; 2003.

91. Brady TJ, Murphy L, O'Colmain BJ, Beauchesne D, Daniels B, Greenberg M, *et al.* A meta-analysis of health status, health behaviors, and health care utilization outcomes of the Chronic Disease Self-Management Program. *Prev Chronic Dis* 2013;**10**:120112. https://doi.org/10.5888/pcd10.120112

92. Centers for Disease Control and Prevention (CDC). *Asthma Facts: CDC's National Asthma Control Program Grantees*. Atlanta, GA: CDC; 2013. URL: austinpureair.com/uploadimage/139828838266969.pdf (accessed 29 June 2019).

93. National Association of County and City Health Officials. *Diabetes Self-Management Education and Training: Fact Sheet – 2013*. Washington, DC: National Association of County and City Health Officials; 2013. http://archived.naccho.org/topics/HPDP/diabetes/resources/upload/factsheet_diabetes_aug2013_v2.pdf (accessed 29 June 2019).

94. Brady TJ, Anderson LA, Kobau R. Chronic disease self-management support: public health perspectives. *Front Public Health* 2014;**2**:234. https://doi.org/10.3389/fpubh.2014.00234

95. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). *National Diabetes Education Program: National Diabetes Survey 2016*. Bethesda, MA: NIDDK; 2016. URL: www.niddk.nih.gov/health-information/health-statistics/diabetes-statistics/ndep-national-diabetes-survey (accessed 29 June 2019).

96. Centers for Disease Control and Prevention (CDC). *Self-management Education Workshops*. 2019. URL: www.cdc.gov/arthritis/interventions/self_manage.htm (accessed 29 June 2019).

97. DAFNE Study Group. Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial. *BMJ* 2002;**325**:746. https://doi.org/10.1136/bmj.325.7367.746

98. Harris SM, Shah P, Mulnier H, Healey A, Thomas SM, Amiel SA, Hopkins D. Factors influencing attendance at structured education for type 1 diabetes in south London. *Diabet Med* 2017;**34**:828–33. https://doi.org/10.1111/dme.13333

99. Bradley PM, Lindsay B, Fleeman N. Care delivery and self management strategies for adults with epilepsy. *Cochrane Database Syst Rev* 2016;**2**:CD006244. https://doi.org/10.1002/14651858.CD006244.pub3

100. Helgeson DC, Mittan R, Tan SY, Chayasirisobhon S. Sepulveda Epilepsy Education: the efficacy of a psychoeducational treatment program in treating medical and psychosocial aspects of epilepsy. *Epilepsia* 1990;**31**:75–82. https://doi.org/10.1111/j.1528-1157.1990.tb05363.x

101. May TW, Pfäfflin M. The efficacy of an educational treatment program for patients with epilepsy (MOSES): results of a controlled, randomized study. Modular Service Package Epilepsy. *Epilepsia* 2002;**43**:539–49. https://doi.org/10.1046/j.1528-1157.2002.23801.x

102. DiIorio C, Bamps Y, Walker ER, Escoffery C. Results of a research study evaluating WebEase, an online epilepsy self-management program. *Epilepsy Behav* 2011;**22**:469–74. https://doi.org/10.1016/j.yebeh.2011.07.030

103. Aliasgharpour M, Dehgahn Nayeri N, Yadegary MA, Haghani H. Effects of an educational program on self-management in patients with epilepsy. *Seizure* 2013;**22**:48–52. https://doi.org/10.1016/j.seizure.2012.10.005

104. Lindsay B, Bradley PM. Care delivery and self-management strategies for children with epilepsy. *Cochrane Database Syst Rev* 2010;**12**:CD006245. https://doi.org/10.1002/14651858.CD006245.pub2

105. Lewis MA, Salas I, de la Sota A, Chiofalo N, Leake B. Randomized trial of a program to enhance the competencies of children with epilepsy. *Epilepsia* 1990;**31**:101–9. https://doi.org/10.1111/j.1528-1157.1990.tb05367.x

106. Lewis MA, Hatton CL, Salas I, Leake B, Chiofalo N. Impact of the Children's Epilepsy Program on parents. *Epilepsia* 1991;**32**:365–74. https://doi.org/10.1111/j.1528-1157.1991.tb04665.x

107. Gibson PG, Powell H, Coughlan J, Wilson AJ, Hensley MJ, Abramson M, *et al.* Limited (information only) patient education programs for adults with asthma. *Cochrane Database Syst Rev* 2002;**2**:CD001005. https://doi.org/10.1002/14651858.CD001005

108. Michaelis R, Tang V, Wagner JL, Modi AC, LaFrance WC, Goldstein LH, *et al.* Psychological treatments for people with epilepsy. *Cochrane Database Syst Rev* 2017;**10**:CD012081. https://doi.org/10.1002/14651858.CD012081.pub2

109. Ramaratnam S, Baker GA, Goldstein LH. Psychological treatments for epilepsy. *Cochrane Database Syst Rev* 2008;**3**:CD002029. https://doi.org/10.1002/14651858.CD002029.pub3

110. Bradley PM, Lindsay B. Care delivery and self-management strategies for adults with epilepsy. *Cochrane Database Syst Rev* 2008;**1**:CD006244. https://doi.org/10.1002/14651858.CD006244.pub2

111. Savovic J, Turner RM, Mawdsley D, Jones HE, Beynon R, Higgins JPT, Sterne JAC. Association between risk-of-bias assessments and results of randomized trials in Cochrane reviews: the ROBES meta-epidemiologic study. *Am J Epidemiol* 2018;**187**:1113–22. https://doi.org/10.1093/aje/kwx344

112. Department of Health and Social Care (DHSC). *The Expert Patient: A New Approach to Chronic Disease Management for the 21st Century*. London: DHSC; 2001.

113. National Clinical Guideline Centre. *The Epilepsies: The Diagnosis and Management of the Epilepsies in Adults and Children in Primary and Secondary Care*. London: National Clinical Guideline Centre; 2011.

114. NHS England. *Living with Epilepsy*. 2017. URL: www.nhs.uk/conditions/epilepsy/pages/living-with.aspx (accessed 14 September 2017).

115. NHS England. *Transforming Urgent and Emergency Care Services in England: Urgent and Emergency Care Review – End of Phase 1 Report*. London: NHS England; 2031. URL: www.nhs.uk/NHSEngland/keogh-review/Documents/UECR.Ph1Report.FV.pdf (accessed 23 August 2019).

116. Michie S, West R, Campbell R. Brown J, Gainforth H. *ABC of Behaviour Change Theories: An Essential Resource for Researchers, Policy Makers and Practitioners*. London: Silverback Publishing; 2014.

117. Morrish PK. Inadequate neurology services undermine patient care in the UK. *BMJ* 2015;**350**:h3284. https://doi.org/10.1136/bmj.h3284

118. Royal College of Physicians (RCP). *Local Adult Neurology Services for the Next Decade: Report of a Working Party*. London: RCP; 2011. URL: www.mstrust.org.uk/sites/default/files/files/Local%20adult%20neurology%20services%20for%20the%20next%20decade.pdf (accessed 29 June 2019).

119. Epilepsy Action. *Best Care: The Value of Epilepsy Specialist Nurses*. Leeds: British Epilepsy Association; 2010.

120. Epilepsy Action. *A Critical Time for Epilepsy in England: A Study of Epilepsy Service Provision in England*. Leeds: British Epilepsy Association; 2013.

121. Medical Research Council (MRC). *A Framework for the Development and Evaluation of RCTs for Complex Interventions to Improve Health*. London: MRC; 2000.

122. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, Tyrer P. Framework for design and evaluation of complex interventions to improve health. *BMJ* 2000;**321**:694–6. https://doi.org/10.1136/bmj.321.7262.694

123. Jain P, Patterson VH, Morrow JI. What people with epilepsy want from a hospital clinic. *Seizure* 1993;**2**:75–8. https://doi.org/10.1016/S1059-1311(05)80106-2

124. Davis KL, Candrilli SD, Edin HM. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. *Epilepsia* 2008;**49**:446–54. https://doi.org/10.1111/j.1528-1167.2007.01414.x

125. Moran N, Poole K, Bell G, Solomon J, Kendall S, McCarthy M, *et al.* NHS services for epilepsy from the patient's perspective: a survey of primary, secondary and tertiary care access throughout the UK. *Seizure* 2000;**9**:559–65. https://doi.org/10.1053/seiz.2000.0451

126. Fraser RT, Johnson EK, Lashley S, Barber J, Chaytor N, Miller JW, *et al.* PACES in epilepsy: results of a self-management randomized controlled trial. *Epilepsia* 2015;**56**:1264–74. https://doi.org/10.1111/epi.13052

127. Laybourne AH, Morgan M, Watkins SH, Goldstein LH. Self-management for people with poorly control-led epilepsy: participants' views of the UK self-management in epilepsy (SMILE) program. *Epil Behav* 2015;**52**:159–64. https://doi.org/10.1016/j.yebeh.2015.08.023

128. Noble AJ, McCrone P, Seed PT, Goldstein LH, Ridsdale L. Clinical- and cost-effectiveness of a nurse led self-management intervention to reduce emergency visits by people with epilepsy. *PLOS ONE* 2014;**9**:e90789. https://doi.org/10.1371/journal.pone.0090789

129. Fraser RT, Johnson EK, Miller JW, Temkin N, Barber J, Caylor L, *et al.* Managing epilepsy well: self-management needs assessment. *Epilepsy Behav* 2011;**20**:291–8. https://doi.org/10.1016/j.yebeh.2010.10.010

130. Donetto S, Pierri P, Tsianakas V, Robert G. Experience-based co-design and healthcare improvement: realising participatory design in the public sector. *Design J* 2015;**18**:227–48. https://doi.org/10.2752/175630615X14212498964312

131. Walters SJ, Bonacho Dos Anjos Henriques-Cadby I, Bortolami O, Flight L, Hind D, Jacques RM, *et al.* Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment programme. *BMJ Open* 2017;**7**:e015276. https://doi.org/10.1136/bmjopen-2016-015276

132. Thabane L, Ma J, Chu R, Cheng J, Ismaila A, Rios LP, *et al.* A tutorial on pilot studies: the what, why and how. *BMC Med Res Methodol* 2010;**10**:1. https://doi.org/10.1186/1471-2288-10-1

133. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. *J Eval Clin Pract* 2004;**10**:307–12. https://doi.org/10.1111/j.2002.384.doc.x

134. Kralj-Hans I, Goldstein LH, Noble AJ, Landau S, Magill N, McCrone P, *et al.* Self-Management education for adults with poorly controlled epILEpsy [SMILE (UK)]: a randomised controlled trial protocol. *BMC Neurol* 2014;**14**:69. https://doi.org/10.1186/1471-2377-14-69

135. Williams B, Skinner J, Dowell J, Roberts R, Crombie I, Davis J. General practitioners' reasons for the failure of a randomized controlled trial (the TIGER trial) to implement epilepsy guidelines in primary care. *Epilepsia* 2007;**48**:1275–82. https://doi.org/10.1111/j.1528-1167.2007.01057.x

136. Patton MQ. *Qualitative Research and Evaluation Methods*. Thousand Oaks, CA: SAGE Publications Ltd; 2002.

137. Cresswell JW, Plano Clark VL. *Designing and Conducting Mixed Method Research*. Thousand Oaks, CA: SAGE Publications Ltd; 2011.

138. Bernard HR. *Research Methods in Anthropology: Qualitative and Quantitative Approaches*. Walnut Creek, CA: Alta Mira Press; 2002.

139. Spradley JP. *The Ethnographic Interview*. New York, NY: Holt, Rinehart & Winston; 1979.

140. Duffield C. The Delphi technique: a comparison of results obtained using two expert panels. *Int J Nurs Stud* 1993;**30**:227–37. https://doi.org/10.1016/0020-7489(93)90033-q

141. Lemmer B. Successive surveys of an expert panel: research in decision making with health visitors *J Adv Nurs* 1998;**27**:538–45. https://doi.org/10.1046/j.1365-2648.1998.00544.x

142. INVOLVE. *Briefing Notes for Researchers: Involving the Public in NHS, Public Health and Social Care Research*. Eastleigh: INVOLVE; 2012.

143. NHS England. *What To Do If Someone Has a Seizure (Fit)*. 2014. URL: www.nhs.uk/Livewell/Epilepsy/Pages/Ifyouseeaseizure.aspx (accessed 19 September 2017).

144. Epilepsy Action. *What To Do When Someone Has a Seizure*. 2016. URL: www.epilepsy.org.uk/info/firstaid (accessed 7 August 2016).

145. Epilepsy Society. *When To Dial 999*. 2012. URL: www.epilepsysociety.org.uk/AboutEpilepsy/Firstaid/Whentodial999 (accessed 8 January 2016).

146. Britten N. Qualitative interviews in medical research. *BMJ* 1995;**311**:251–3. https://doi.org/10.1136/bmj.311.6999.251

147. Mishler EG. *Research Interviewing Context and Narrative*. London: Harvard University Press; 1986.

148. Steele CM. The psychology of self-affirmation: sustaining the integrity of the self. In Berkowitz L, editor. *Advances in Experimental Social Psychology*. New York, NY: Academic Press; 1988. pp. 261–302. https://doi.org/10.1016/S0065-2601(08)60229-4

149. Epton T, Harris PR. Self-affirmation promotes health behavior change. *Health Psychol* 2008;**27**:746–52. https://doi.org/10.1037/0278-6133.27.6.746

150. Reed MB, Aspinwall MG. Self-affirmation reduces biased processing of health-risk information. *Motiv Emot* 1998;**22**:99–132. https://doi.org/10.1023/A:1021463221281

151. Armitage CJ, Rowe R. Testing multiple means of self-affirmation. *Br J Psychol* 2011;**102**:535–45. https://doi.org/10.1111/j.2044-8295.2010.02014.x

152. Schüz N, Schüz B, Eid M. When risk communication backfires: randomized controlled trial on self-affirmation and reactance to personalized risk feedback in high-risk individuals. *Health Psychol* 2013;**32**:561–70. https://doi.org/10.1037/a0029887

153. Cohen GL, Sherman DK. The psychology of change: self-affirmation and social psychological intervention. *Annu Rev Psychol* 2014;**65**:333–71. https://doi.org/10.1146/annurev-psych-010213-115137

154. Bazeley P, Richards L, editors. *The NVivo Qualitative Project Book*. London: SAGE Publications Ltd; 2000. https://doi.org/10.4135/9780857020079

155. Skinner TC, Carey ME, Cradock S, Dallosso HM, Daly H, Davies MJ, *et al.* 'Educator talk' and patient change: some insights from the DESMOND (Diabetes Education and Self Management for Ongoing and Newly Diagnosed) randomized controlled trial. *Diabet Med* 2008;**25**:1117–20. https://doi.org/10.1111/j.1464-5491.2008.02492.x

156. Medical Research Council (MRC). *Developing and Evaluating Complex Interventions*. URL: https://mrc.ukri.org/documents/pdf/complex-interventions-guidance (accessed 6 January 2016).

157. Möhler R, Köpke S, Meyer G. Criteria for Reporting the Development and Evaluation of Complex Interventions in healthcare: revised guideline (CReDECI 2). *Trials* 2015;**16**:204. https://doi.org/10.1186/s13063-015-0709-y

158. Public Health England (PHE). *Local Health Profiles 2015: Liverpool*. London: PHE; 2015. URL: https://fingertips.phe.org.uk/profile/health-profiles/data#page/1/gid/1938133217/pat/6/par/E12000002/ati/202/are/E08000012/iid/91872/age/1/sex/4/cid/4/page-options/cin-ci-4_ine-vo-0_ine-ct-9_ine-yo-3: 2010:-1:-1_ine-pt-0_eng-vo-0_eng-do-0_car-do-0_ovw-do-0 (accessed 10 August 2020).

159. Public Health England (PHE). *Local Health Profiles 2015: Wirral*. London: PHE; 2015. URL: https://fingertips.phe.org.uk/profile/health-profiles/data#page/1/gid/1938133217/pat/6/par/E12000002/ati/202/are/E08000015/iid/91872/age/1/sex/4/cid/4/page-options/cin-ci-4_ine-vo-0_ine-ct-9_ine-yo-3: 2010:-1:-1_ine-pt-0_eng-vo-0_eng-do-0_car-do-0_ovw-do-0 (accessed 10 August 2020).

160. NHS Digital. *Quality and Outcomes Framework (QOF) 2012–13*. Leeds: NHS Digital; 2013. URL: https://digital.nhs.uk/data-and-information/publications/statistical/quality-and-outcomes-framework-achievement-prevalence-and-exceptions-data/quality-and-outcomes-framework-2012-13 (accessed 10 August 2020).

161. NHS Digital. *Hospital Accident and Emergency Activity: Supporting Information 2017-18*. Leeds: NHS Digital; 2018. URL: https://files.digital.nhs.uk/8B/94BB9E/AE1718_supporting_information.pdf (accessed 27 August 2019).

162. Kahan BC, Morris TP. Reporting and analysis of trials using stratified randomisation in leading medical journals: review and reanalysis. *BMJ* 2012;**345**:e5840. https://doi.org/10.1136/bmj.e5840

163. Mittan R. Fear of Seizures. In S. Whitman, B. Hermann, editors. *Psychopathology in Epilepsy: Social Dimensions*. New York, NY: Oxford University Press; 1986. pp. 90–121.

164. Martiniuk AL, Speechley KN, Secco M, Karen Campbell M. Development and psychometric properties of the Thinking about Epilepsy questionnaire assessing children's knowledge and attitudes about epilepsy. *Epilepsy Behav* 2007;**10**:595–603. https://doi.org/10.1016/j.yebeh.2007.01.011

165. Shore CP, Austin JK, Dunn DW. Maternal adaptation to a child's epilepsy. *Epilepsy Behav* 2004;**5**:557–68. https://doi.org/10.1016/j.yebeh.2004.04.015

166. Cramer JA, Perrine K, Devinsky O, Bryant-Comstock L, Meador K, Hermann B. Development and cross-cultural translations of a 31-item quality of life in epilepsy inventory. *Epilepsia* 1998;**39**:81–8. https://doi.org/10.1111/j.1528-1157.1998.tb01278.x

167. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**:361–70. https://doi.org/10.1111/j.1600-0447.1983.tb09716.x

168. Snaith P. What do depression rating scales measure? *Br J Psychiatry* 1993;**163**:293–8. https://doi.org/10.1192/bjp.163.3.293

169. Thapar A, Kerr M, Harold G. Stress, anxiety, depression, and epilepsy: investigating the relationship between psychological factors and seizures. *Epilepsy Behav* 2009;**14**:134–40. https://doi.org/10.1016/j.yebeh.2008.09.004

170. Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. *Gerontologist* 1980;**20**:649–55. https://doi.org/10.1093/geront/20.6.649

171. Beecham J, Knapp M. Costing Psychiatric Interventions. In Thornicroft G, Brewin C, Wing J, editors. *Measuring Mental Health Needs*. London: Gaskell; 1992. pp. 163–83.

172. Williams A. *The Role of the EUROQOL Instrument in QALY Calculations*. York: Centre for Health Economics, University of York; 1995.

173. Smyth RM, Duley L, Jacoby A, Elbourne D. Women's experiences of participating in the Magpie Trial: a postal survey in the United Kingdom. *Birth* 2009;**36**:220–9. https://doi.org/10.1111/j.1523-536X.2009.00326.x

174. Powell GA, Bonnett LJ, Tudur-Smith C, Hughes DA, Williamson PR, Marson AG. Using routinely recorded data in the UK to assess outcomes in a randomised controlled trial: The Trials of Access. *Trials* 2017;**18**:389. https://doi.org/10.1186/s13063-017-2135-9

175. Noble AJ, Marson AG. Which outcomes should we measure in adult epilepsy trials? The views of people with epilepsy and informal carers. *Epilepsy Behav* 2016;**59**:105–10. https://doi.org/10.1016/j.yebeh.2016.01.036

176. NHS Digital. *Accident and Emergency Attendances in England 2012–13*. Leeds: NHS Digital; 2014. URL: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-accident–emergency-activity/accident-and-emergency-attendances-in-england-2012-13 (accessed 4 August 2019).

177. Bhatt H, Matharu MS, Henderson K, Greenwood R. An audit of first seizures presenting to an accident and emergency department. *Seizure* 2005;**14**:58–61. https://doi.org/10.1016/j.seizure.2004.10.003

178. Ridsdale L, McCrone P, Morgan M, Goldstein L, Seed P, Noble A. Can an epilepsy nurse specialist-led self-management intervention reduce attendance at emergency departments and promote well-being for people with severe epilepsy? A non-randomised trial with a nested qualitative phase. *Health Serv Deliv Res* 2013;**1**(9). https://doi.org/10.3310/hsdr01090

179. Brueton VC, Tierney JF, Stenning S, Meredith S, Harding S, Nazareth I, Rait G. Strategies to improve retention in randomised trials: a Cochrane systematic review and meta-analysis. *BMJ Open* 2014;**4**:e003821. https://doi.org/10.1136/bmjopen-2013-003821

180. Vuong Q. Likelihood ratio tests for model selection and non-nested hypotheses. *Econometrica* 1989;**57**:307–33. https://doi.org/10.2307/1912557

181. Lee EC, Whitehead AL, Jacques RM, Julious SA. The statistical interpretation of pilot trials: should significance thresholds be reconsidered? *BMC Med Res Methodol* 2014;**14**:41. https://doi.org/10.1186/1471-2288-14-41

182. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;**1**:307–10. https://doi.org/10.1016/S0140-6736(86)90837-8

183. Keene ON, Jones MR, Lane PW, Anderson J. Analysis of exacerbation rates in asthma and chronic obstructive pulmonary disease: example from the TRISTAN study. *Pharm Stat* 2007;**6**:89–97. https://doi.org/10.1002/pst.250

184. Cramer JA, Van Hammée G, N132 Study Group. Maintenance of improvement in health-related quality of life during long-term treatment with levetiracetam. *Epilepsy Behav* 2003;**4**:118–23. https://doi.org/10.1016/S1525-5050(03)00004-0

185. Bell ML, Fairclough DL, Fiero MH, Butow PN. Handling missing items in the Hospital Anxiety and Depression Scale (HADS): a simulation study. *BMC Res Notes* 2016;**9**:479. https://doi.org/10.1186/s13104-016-2284-z

186. Austin JK, Dunn DW, Johnson CS, Perkins SM. Behavioral issues involving children and adolescents with epilepsy and the impact of their families: recent research data. *Epilepsy Behav* 2004;**5**(Suppl. 3):33–41. https://doi.org/10.1016/j.yebeh.2004.06.014

187. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, *et al.* Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;**348**:g1687. https://doi.org/10.1136/bmj.g1687

188. Coffman JM, Cabana MD, Halpin HA, Yelin EH. Effects of asthma education on children's use of acute care services: a meta-analysis. *Pediatrics* 2008;**121**:575–86. https://doi.org/10.1542/peds.2007-0113

189. Wojewodka G, Hurley S, Taylor SJC, Noble AJ, Ridsdale L, Goldstein LH. Implementation fidelity of a self-management course for epilepsy: method and assessment. *BMC Med Res Methodol* 2017;**17**:100. https://doi.org/10.1186/s12874-017-0373-x

190. Lausberg H, Sloetjes H. Coding gestural behavior with the NEUROGES – ELAN system. *Behav Res Methods* 2009;**41**:841–9. https://doi.org/10.3758/BRM.41.3.841

191. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *J Chiropr Med* 2016;**15**:155–63. https://doi.org/10.1016/j.jcm.2016.02.012

192. Feinstein AR, Cicchetti DV. High agreement but low kappa: I. The problems of two paradoxes. *J Clin Epidemiol* 1990;**43**:543–9. https://doi.org/10.1016/0895-4356(90)90158-L

193. Byrt T, Bishop J, Carlin JB. Bias, prevalence and kappa. *J Clin Epidemiol* 1993;**46**:423–9. https://doi.org/10.1016/0895-4356(93)90018-V

194. NHS England. *AE Waiting Times and Activities*. 2015. URL: www.england.nhs.uk/statistics/statistical-work-areas/ae-waiting-times-and-activity/statistical-work-areasae-waiting-times-and-activityae-attendances-and-emergency-admissions-2015-16-monthly-3/ (accessed 27 August 2019).

195. Glick HA, Doshi JA, Sonnad SS, Polsky D. *Economic Evaluation in Clinical Trials*. Oxford: Oxford University Press; 2014. https://doi.org/10.1093/med/9780199685028.001.0001

196. Sach TH, Desborough J, Houghton J, Holland R, CAREMED study team. Applying micro-costing methods to estimate the costs of pharmacy interventions: an illustration using multi-professional clinical medication reviews in care homes for older people. *Int J Pharm Pract* 2015;**23**:237–47. https://doi.org/10.1111/ijpp.12162

197. Lopetegui M, Yen PY, Lai A, Jeffries J, Embi P, Payne P. Time motion studies in healthcare: what are we talking about? *J Biomed Informat* 2014;**49**:292–99. https://doi.org/10.1016/j.jbi.2014.02.017

198. University of Liverpool. *Salary, Scales and Hourly Rates 2017–18*. 2018. URL: www.liverpool.ac.uk/media/livacuk/hr/working/Salary,Scales,and,Hourly,Rates,2017–18.pdf (accessed 30 April 2018).

199. BT. *BT Business Phone Line Call Charges*. URL: https://business.bt.com/content/dam/bt/business/PDFs/phonelines/BT-Business-Call-Charges.pdf (accessed 30 August 2018).

200. Royal Liverpool Academy. *Room Capacity & Charges*. URL: www.royalliverpoolacademy.nhs.uk/media/2777/room-charges-0417-pdf.pdf (accessed 30 August 2018).

201. Royal Mail. *Response Rate Card*. URL: www.royalmail.com/business/system/files/Response-Services-rate-card-March-2018–138.pdf (accessed 30 August 2018).

202. Ioannidis JP. How to make more published research true. *PLOS Med* 2014;**11**:e1001747. https://doi.org/10.1371/journal.pmed.1001747

203. Ridsdale L, Robins D, Cryer C, Williams H. Feasibility and effects of nurse run clinics for patients with epilepsy in general practice: randomised controlled trial. Epilepsy Care Evaluation Group. *BMJ* 1997;**314**:120–2. https://doi.org/10.1136/bmj.314.7074.120

204. Warren E, Baker GA, Campion P, Chadwick DR, Jacoby A, Luker K. *An Evaluation of a Nurse Specialist Case Manager Intervention in the Management of Epilepsy*. Report for the North West Regional Health Authority, R&D Directorate; 1998.

205. Helde G, Bovim G, Bråthen G, Brodtkorb E. A structured, nurse-led intervention program improves quality of life in patients with epilepsy: a randomized, controlled trial. *Epilepsy Behav* 2005;**7**:451–7. https://doi.org/10.1016/j.yebeh.2005.06.008

206. Monfared AA, Lelorier J. Accuracy and validity of using medical claims data to identify episodes of hospitalizations in patients with COPD. *Pharmacoepidemiol Drug Saf* 2006;**15**:19–29. https://doi.org/10.1002/pds.1131

207. Roberts RO, Bergstralh EJ, Schmidt L, Jacobsen SJ. Comparison of self-reported and medical record health care utilization measures. *J Clin Epidemiol* 1996;**49**:989–95. https://doi.org/10.1016/0895-4356(96)00143-6

208. Ridsdale L, Wojewodka G, Robinson EJ, Noble AJ, Morgan M, Taylor SJC, *et al.* The effectiveness of a group self-management education course for adults with poorly controlled epilepsy, SMILE (UK): a randomized controlled trial. *Epilepsia* 2018;**59**:1048–61. https://doi.org/10.1111/epi.14073

209. Raftery J, Young A, Stanton L, Milne R, Cook A, Turner D, Davidson P. Clinical trial metadata: defining and extracting metadata on the design, conduct, results and costs of 125 randomised clinical trials funded by the National Institute for Health Research Health Technology Assessment programme. *Health Technol Assess* 2015;**19**(11). https://doi.org/10.3310/hta19110

210. Hassan TB, Walker B, Harrison M, Rae F. *Stretched to the Limit: A Survey of Emergency Medicine Consultants in the UK*. London: College of Emergency Medicine; 2013. URL: www.rcem.ac.uk/docs/Policy/CEM7461-Stretched-to-the-limit-October_2013.pdf (accessed 29 June 2019).

211. Medical Research Council (MRC). *Obtaining Data from NHS Digital*. https://mrc.ukri.org/documents/pdf/obtaining-nhs-digital-data-guidance-v300317/ (accessed 3 September 2020).

212. Ridsdale L, McKinlay A, Wojewodka G, Robinson EJ, Mosweu I, Feehan SJ, *et al.* Self-Management education for adults with poorly controlled epILEpsy [SMILE (UK)]: a randomised controlled trial. *Health Technol Assess* 2018;**22**(21). https://doi.org/10.3310/hta22210

213. 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. https://doi.org/10.1111/j.1528-1157.1997.tb01128.x

214. Scambler G, Hopkins A. Becoming epileptic: coming to terms with stigma. *Social Health Ill* 1986;**8**:22–43. https://doi.org/10.1111/1467-9566.ep11346455

215. Department of Health and Social Care (DHSC). *The NHS Constitution for England*. 2015. URL: www.gov.uk/government/publications/the-nhs-constitution-for-england/the-nhs-constitution-for-england (accessed 27 August 2019).

216. NHS England. *Emergency Care Data Set*. London: NHS England; 2015. URL: www.england.nhs.uk/wp-content/uploads/2015/08/em-care-data-set.pdf (accessed 27 August 2019).

217. NHS Digital. *CDS Type 011: Emergency Care Data Set (ECDS) User Guidance*. Leeds: NHS Digital; 2017. URL: https://digital.nhs.uk/data-and-information/data-collections-and-data-sets/data-sets/emergency-care-data-set-ecds/ecds-guidance (accessed 15 July 2019).

218. NHS Digital. *ECDS FAQ: May 2017 Emergency Care Data Set Frequently Asked Questions*. Leeds: NHS Digital; 2017 URL: https://digital.nhs.uk/binaries/content/assets/legacy/pdf/j/1/ecds_implementation_faqs_v1.0.pdf (accessed 15 July 2019).

219. Luedke MW, Blalock DV, Lewinski AA, Shapiro A, Drake C, Lewis JD, *et al. Self-management of Epilepsy: A Systematic Review*. Washington, DC: US Department of Veteran Affairs; 2019. https://doi.org/10.7326/M19-0458

220. Sajatovic M, Colon-Zimmermann K, Kahriman M, Fuentes-Casiano E, Liu H, Tatsuoka C, *et al.* A 6-month prospective randomized controlled trial of remotely delivered group format epilepsy self-management versus waitlist control for high-risk people with epilepsy. *Epilepsia* 2018;**59**:1684–95. https://doi.org/10.1111/epi.14527

221. Snape D, Kirkham J, Britten N, Froggatt K, Gradinger F, Lobban F, *et al.* Exploring perceived barriers, drivers, impacts and the need for evaluation of public involvement in health and social care research: a modified Delphi study. *BMJ Open* 2014;**4**:e004943. https://doi.org/10.1136/bmjopen-2014-004943

222. Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, Lancaster GA, PAFS consensus group. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ* 2016;**355**:i5239. https://doi.org/10.1136/bmj.i5239

223. Noble AJ, Marson AG, Blower SL. Psychological interventions for epilepsy: How good are trialists at assessing their implementation fidelity, what are the barriers, and what are journals doing to encourage it? A mixed methods study. *Epilepsy Behav* 2019;**97**:174–81. https://doi.org/10.1016/j.yebeh.2019.05.041

224. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, *et al.* Process evaluation of complex interventions: Medical Research Council guidance. *BMJ* 2015;**350**:h1258. https://doi.org/10.1136/bmj.h1258

225. Perepletchikova F, Hilt LM, Chereji E, Kazdin AE. Barriers to implementing treatment integrity procedures: survey of treatment outcome researchers. *J Consult Clin Psychol* 2009;**77**:212–18. https://doi.org/10.1037/a0015232

226. Kobau R, Price P. Knowledge of epilepsy and familiarity with this disorder in the US population: results from the 2002 HealthStyles Survey. *Epilepsia* 2003;**44**:1449–54. https://doi.org/10.1046/j.1528-1157.2003.17603.x

227. Faught E, Duh MS, Weiner JR, Guérin A, Cunnington MC. Nonadherence to antiepileptic drugs and increased mortality: findings from the RANSOM Study. *Neurology* 2008;**71**:1572–8. https://doi.org/10.1212/01.wnl.0000319693.10338.b9

228. Tan JH, Wilder-Smith E, Lim EC, Ong BK. Frequency of provocative factors in epileptic patients admitted for seizures: a prospective study in Singapore. *Seizure* 2005;**14**:464–9. https://doi.org/10.1016/j.seizure.2005.07.010

229. Mitchell WG, Conry JA, Crumrine PK, Kriel RL, Cereghino JJ, Groves L, Rosenfeld WE. An open-label study of repeated use of diazepam rectal gel (Diastat) for episodes of acute breakthrough seizures and clusters: safety, efficacy, and tolerance. North American Diastat Group. *Epilepsia* 1999;**40**:1610–17. https://doi.org/10.1111/j.1528-1157.1999.tb02047.x

230. O'Dell C, Shinnar S, Ballaban-Gil KR, Hornick M, Sigalova M, Kang H, Moshé SL. Rectal diazepam gel in the home management of seizures in children. *Pediatr Neurol* 2005;**33**:166–72. https://doi.org/10.1016/j.pediatrneurol.2005.03.005

231. Stavem K, Bjørnaes H, Lossius MI. Properties of the 15D and EQ-5D utility measures in a community sample of people with epilepsy. *Epilepsy Res* 2001;**44**:179–89. https://doi.org/10.1016/S0920-1211(01)00201-7

232. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;**52**:69–77. https://doi.org/10.1016/S0022-3999(01)00296-3

233. Taylor SJC, Pinnock H, Epiphaniou E, Pearce G, Parke HL, Schwappach A, *et al.* A rapid synthesis of the evidence on interventions supporting self-management for people with long-term conditions: PRISMS – Practical systematic RevIew of Self-Management Support for long-term conditions. *Health Serv Deliv Res* 2014;**2**(53). https://doi.org/10.3310/hsdr02530

234. Shore CP, Perkins SM, Austin JK. The Seizures and Epilepsy Education (SEE) program for families of children with epilepsy: a preliminary study. *Epilepsy Behav* 2008;**12**:157–64. https://doi.org/10.1016/j.yebeh.2007.10.001

235. Baumeister RF. Self-regulation and Ego-threat: Motivated Cognition, Self-deception, and Destruction in Goal Setting. In Gollwitzer PM, Bargh JA, editors. *The Psychology of Action: Linking Cognition and Motivation to Behavior*. New York, NY: Guilford Press; 1996. pp. 27–47.

236. Morgan SR, Chang AM, Alqatari M, Pines JM. Non-emergency department interventions to reduce ED utilization: a systematic review. *Acad Emerg Med* 2013;**20**:969–85. https://doi.org/10.1111/acem.12219

237. Great Britain. *Medicines for Human Use (Clinical Trials) Regulations 2004*. London: The Stationery Office; 2004. URL: www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf (accessed 10 August 2020).

Appendix 1 Possible ways that the SAFE course could reduce unnecessary/avoidable emergency department use

Primary putative mechanisms	
Low seizure management confidence and skills	**How might the course address and reduce ED use?**
PWE can have low levels of knowledge of epilepsy and seizures, have incorrect beliefs concerning first aid, lack confidence managing seizures and be disproportionately fearful (e.g. Long *et al.*[70]). Consequently, some patients can routinely call for emergency medical assistance when they are about to have or have had a seizure, regardless of whether or not it is medically required	Topics covered in the ES course could increase patients' knowledge of what seizures are, what seizures' effects are and help patients to know when it is necessary to seek emergency assistance. This could serve to increase patients' confidence in managing seizures, including post-ictal states, and help them to delineate the circumstances that require emergency services. The course could also help allay disproportionate fears
Responsibility for managing epileptic seizures is often delegated to SOs (Walker *et al.*[73]). Some have low levels of epilepsy knowledge, have incorrect beliefs concerning seizure first aid, lack of confidence in managing seizures and can be fearful of seizures and their threat to a patient's life (Kobau *et al.*[226]). Consequently, some SOs call for emergency medical attention when the patient has or has had a seizure, regardless of whether or not it is medically required	The ES course could help increase SOs' knowledge of what seizures are, what seizures' effects are and help them to know when it is necessary to seek emergency medical attention and identify alternative pathways of support. It could also help allay disproportionate fears held by the SO The topics covered in the ES course could also help PWE feel more informed and comfortable with their diagnosis. This could empower them to have a discussion with others in their caring network about epilepsy, relay correct information about how they can be helped if they have a seizure and what their preferences are regarding transportation to ED. To help PWE to do this, the ES has a variety of resources that participants are given or have their attention drawn to. For example, in the participant take-away information pack there are a number of free wallet-sized 'seizure first aid cards' that can be given to friends and family members
Secondary putative mechanisms	
Suboptimal medication or risk management	**How might the course address and reduce ED use?**
Evidence that in some cases ED attendance by PWE may have been precipitated by the person having experienced a seizure or seizure-related injury because they have not managed their medication (e.g. have skipped doses) or epilepsy in an optimum manner or managed risk (e.g. not taken precaution to avoid a seizure trigger) (Faught *et al.*;[227] Tan *et al.*[228])	The ES course describes what antiepileptic medications do, explains why adhering to prescribed regimes is important and outlines potential seizure triggers. This could promote better medication and risk management by PWE and so reduce avoidable seizures and associated complications. Imparting this information to SOs could also be helpful and allow them to become powerful supporters of the development of self-management responsibility in the PWE they know (e.g. helping PWE with reminders) and risk management (e.g. helping the PWE to identify and avoid triggers, such as sleep deprivation and stress) The ES course also briefly covers issues to do with the commonality of epilepsy, whom it affects and its emotional impact, provides participants with the contact details of support agencies and helps to dispel some misconceptions and myths about epilepsy (e.g. its causes). This, along with meeting other PWE, may help reduce feelings of stigma and shame about the diagnosis. Stigma can be associated with willingness to accept one's diagnosis and antiepileptic treatments

Lack of emergency seizure medication	How might the course address and reduce ED use?
Portable emergency seizure medications (e.g. buccal midazolam) are suitable for some PWE. They can be prescribed to PWE who have had a previous episode of prolonged or serial convulsive seizures (NICE).[49] They can empower patients and families to manage some seizures, without the need for medical assistance (Mitchell *et al.*;[229] O'Dell *et al.*[230]). However, patients and SOs might not be aware of them or their utility. They may also have incorrect beliefs about them (e.g. that all need to be rectally administered), which could act as a barrier to their use	The ES course covers emergency medication. Sources of further information on this topic are also provided. The information could enable PWE to start a discussion with usual care providers about whether or not such treatment is suitable for them
Lack of epilepsy identification at time of seizure	**How might the course address and reduce ED use?**
In a minority of cases (≈ 15%; Reuber *et al.*[23]), ED visits by PWE occur because the person is alone, has an uncomplicated seizure in a public place and a bystander calls for an ambulance. Evidence indicates that it can be challenging for ambulance staff to know whether or not it is safe to discharge the patient at the scene because they do not know the patient's medical history. The patient may also be post-ictal; although it is not necessary to transport them to hospital, they do not have an alternative way of ensuring patient safety. Some evidence indicates that low confidence in managing seizures results in some ambulance staff being insistent about transporting the patient to ED (Burrell *et al.*[78])	The ES course does not currently cover this topic. However, with the help of experts and users consulted during the development phase, it might be feasible to introduce this as a new topic. This could involve briefly discussing with PWE and SOs the challenges that face ambulance crews when managing seizures, the benefits of patients carrying easily accessible epilepsy identification cards and the benefits of patients carrying the contact details of a SO who could be contacted to look after the patient and explain the patient's medical history. Patients could also be advised on the rules and regulations concerning transportation to ED by paramedics

Appendix 2 Participant information sheet for health-care professional representatives (part A)

PARTICIPANT INFORMATION SHEET

Study title: Research to design a course on seizure first aid for people with epilepsy and their family and friends

(REC reference no: 15/NW/0225)

1. Invitation paragraph

You are being asked to take part in a research study. Here is information to help you decide if you want to take part.

Please read it carefully. Ask us if there is anything you do not understand or if you want more information. You can take time to decide whether or not you want to take part.

2. The background to the study

Currently, 6 out of 7 hospital admissions for epilepsy are made on an emergency, rather than planned basis. Many of these visits have little long term benefit for patients as the seizures leading to them were uncomplicated and occurred in those in whom the diagnosis was already established. Moreover, these emergency visits do not typically lead to people with epilepsy receiving any additional ongoing support from the NHS.

One reason why people with epilepsy visit emergency departments for uncomplicated seizures is that they and their informal carers can lack confidence managing seizures. They can be unsure as to what the effects of seizures are, not know when medical attention is required, and can be fearful of death. As you will know, the NHS has not yet implemented routine education for people diagnosed with epilepsy and there is limited time within usual care appointments for this information to be provided.

Therefore, in partnership with the Epilepsy Society, our project aims to develop a short, group-based course on seizure first aid. It will be specifically designed for adults with established epilepsy who frequently make emergency visits and their family and friends. Once developed, we shall complete a pilot trial of the course.

3. How do you want people like me to be involved?

Rather than starting from scratch, the course that we will develop shall be based on a successful ½-day group course offered by the Epilepsy Society. Their course is titled 'Epilepsy awareness and seizure management'. People from a variety of backgrounds, including patients, carers, teachers and care home staff, pay to attend their course. It is delivered by an educational facilitator who has experience of working with people with epilepsy, such as a nurse.

The Society's course was not specifically developed to meet the needs of people with epilepsy who visit emergency departments. This group can be particularly challenged by epilepsy and may have lower educational levels. We therefore need to adapt the course, refining its content and format for the target population.

To help us do this, we are seeking advice on what changes are needed to the current course from representatives from the main groups and sectors supporting people with epilepsy. We shall also consult with patients and carers.

4. Why am I being invited to take part?

The groups we shall seek feedback from includes the ambulance service, neurologists, nurses, general practitioners, and emergency medicine doctors. We shall also speak with representatives from user groups and the commissioning sector. We believe your expertise makes you well placed to provide us with feedback on the course.

5. If I agreed to take part what would I have to do?

You would be sent the content and materials for the Epilepsy Society's current package and their guidelines on what constitutes appropriate first aid for seizures. Then ~2 weeks later you will be asked to provide feedback by means of an interview with our research worker. The interview would last about 60 minutes.

Depending on your preference, the interview will be conducted face-to-face, by telephone or by Skype. The things that we would like your feedback on will vary depending on your area of expertise. If you are medically trained, questions might include:

- "What did and didn't you like about the course's current content and delivery?"
- "What inaccuracies are there in the content of the current course?"
- "How do you suggest the programme could be more helpful?"
- "How do you think the intervention might be best rolled out within the NHS, if a future trial found it to be effective?"

6. Do I have to take part?

No. It is up to you. If you want to take part, you will be given this information sheet to keep, given the opportunity to have any questions answered and asked to sign a consent form.

If you decide to take part, you are free to change your mind at any time and you will not need to give a reason. No new information would be collected from you. However, any information that had already been collected would typically be kept by the study team.

7. Are there any benefits in taking part?

The information we get from the study may help us better support people with epilepsy in the future.

To recognise the time and effort involved in reviewing the course materials and in providing feedback you will receive a consultancy fee of £200.

8. Are there any risks in taking part?

There are no known disadvantages or risks of taking part.

9. Will my taking part be kept confidential?

Yes. Only the research team will be able to see the information. This includes the audio recording from your interview. Anything that we publish or pass on will have your name and address and any personal information removed so that you cannot be identified. All information will be stored on password protected computers at the University of Liverpool.

10. What if something goes wrong?

The University of Liverpool provides insurance cover just in case you experience a problem from taking part in the study. If you are worried about anything to do with the study, you should contact the research team. Their details are at the end of this sheet.

11. What will happen to the results of the study?

The results from this study will be used to identify what changes are needed to the Epilepsy Society's current course. They might also be published. You will not be identified in any report. If you would like to have a copy of any published results, you can ask for one by contacting the study team.

All information generated by this study, including the transcriptions from the interviews, will be held on password secured computers at the University of Liverpool offices. In line with the university's policy, data will be archived at the University of Liverpool for of at least 10 years, longer if judged to be of historical significance. After this period the data will be destroyed.

12. Who is funding and organising the study?

The study is funded by the National Institute for Health Research. The study is being done by the Institute of Psychology, Health and Society, The Whelan Building, University of Liverpool, L69 3GL. The lead researcher is Dr Adam Noble.

13. Who has reviewed the study?

This study has been reviewed and approved by National Research Ethics Service Committee North West - Liverpool East (Reference: 15/NW/0225).

14. Contact for further information:

Should you need further information about the study you can contact the research team at any time:

XXXXXXXXXX

You will be given a copy of this information sheet and a signed copy of your consent form to keep.

Appendix 3 Participant information sheet for service user representatives (part A)

PARTICIPANT INFORMATION SHEET

Study title: Research to design a course on seizure first aid for people with epilepsy and their family and friends

(REC reference no: 15/NW/0225)

1. Invitation paragraph

You are being asked to take part in a research study. Before you decide whether you want to take part, it is important for you to know why the research is being done and what it will involve.

Please read this information sheet carefully. If you wish to, you can talk about it with your friends and relatives. Ask us if there is anything you do not understand or if you want more information. You can take time to decide whether you want to take part.

2. What is the reason for the study?

People with epilepsy need to know what to do when a seizure happens. They also need to be able to tell others what to do. This is also true for the friends and family of people with epilepsy.

To feel confident to do these things, some people with epilepsy and family members have said they need more information about epilepsy and seizure first aid. They said they want to know more about the effects of seizures, how to deal with different types of seizures and know when they do and do not need emergency medical help.

Therefore, together with the *Epilepsy Society*, we have made a short course on seizure first aid that people with epilepsy and their family and friends can go on. The course is called Seizure First Aid Training.

Ambulance staff, neurologists, nurses and emergency medicine doctors helped us decide what information the course should give.

We now need to run some practice courses to find out what people with epilepsy and their family and friends think of the course. This will help us know if any parts of the course need changing to make sure it is as good as it can be.

3. Why am I being invited to take part?

We are looking for people with epilepsy to come to one of our practice courses in Liverpool with a family member or friend.

To take part in our study, people with epilepsy need to be aged 16 or over. They must have been diagnosed with epilepsy for 1 or more years and be prescribed anti-epileptic medication. They also need to have visited a hospital emergency department for epilepsy at some point during the last few years. The person can have any type of epilepsy and their seizures can be of any severity. As the Seizure First Aid Training course is given in English people only take part if they can speak, read and understand English well.

You are being invited to take part because we believe you fit this description. You, or a person that you know, contacted us after seeing our advert for participants.

4. Do I have to take part?

No. It is up to you. If you want to take part, you will be given this information sheet to keep, given the opportunity to have any questions answered and asked to sign a consent form.

If you decide to take part, you are free to change your mind at any time and you will not need to give a reason. A decision to stop taking part will not affect the standard of medical care you receive. No new information would be collected on you. However, any information that had already been collected would be kept by the study team.

5. What will happen to me if I take part?

If you agree to take part, a researcher will contact you to get you to sign a consent form. They will arrange for you and one of your family members or friends to come to one of the practice courses.

The course will happen in [INSERT MONTH] of this year. They last about 3 hours and will be held at the [INSERT NAME] centre. This is a specially designed centre for those with conditions like epilepsy. It is [INSERT SUMMARY OF LOCATION].

Each course will be given by a specially trained health professional from the charity, the *Epilepsy Society*. These people are typically nurses and will be able to help should a seizure happen.

The course will be run on a weekday. For the course you will need to go to the centre just once. The courses will typically start at [INSERT TIME] and finish at [INSERT TIME], with breaks included.

The research team will speak with you to find a course that is convenient for you to come to.

About 10 people with epilepsy and their family and friends will be at each of the courses.

During the course, the health professional will give lots of information about epilepsy and show some video clips. The things that the course will cover include:

- How common epilepsy is
- Its causes and some myths about epilepsy
- The tests doctors use to diagnose it
- The different types of seizures and their effects
- How to deal with different seizures, including when to call an ambulance and how to help paramedics help you
- How to improve your confidence and tell others what to do if a person with epilepsy has a seizure.

At the course, you can ask questions. If you want to, you can also share your experiences with the other people.

Everyone taking the course is given an information pack to keep. It includes all the things talked about on the course. It also gives the details of support organisations.

As we have said, the main reason for this study is to see if any part of the Seizure First Aid Training course needs changing to make it better. To help us do this, we want to hear participants' views of the course. Therefore, straight after the course, our researcher will spend about an hour with you and the rest of the group to hear your thoughts. This group talk will be audio-recorded to give an accurate record of the conversation.

6. Expenses

We do not expect that you will have any expenses from taking part in our study. If needed, we can pay for a taxi to take you and your family member or friend to and from the course. We will also provide refreshments for you. Each participant will also receive a £10 shopping voucher to thank them for their time and effort.

If you decide to take time off work to go on the course, we will not be able to pay you or your employer.

7. Are there any benefits in taking part?

We hope you and your family member or friend will get helpful information on epilepsy and learn some things that may increase your confidence to deal with seizures. However, this cannot be guaranteed. The information we get from the study may help us better support people with epilepsy in the future.

8. Are there any risks in taking part?

There are no known risks of taking part.

Taking part in the study will not change the care you get for epilepsy. Your medicines will stay the same and you will see your usual doctors and nurses as normal.

The Seizure First Aid Training course and the group chat afterwards will involve thinking about epilepsy and feelings. For some people, this may be upsetting. You can stop taking part in the course or the group chat at any time. This would not affect your medical care.

If taking part in the study makes you worried about your feelings, you could talk to your GP. You can also ask the health professional giving your course for advice. However, they would not be able to refer you to any NHS service themselves.

9. Will my taking part in this study be kept confidential?

Yes. Anything that we publish or pass on will have your name and address and any personal information removed so that you cannot be identified. All information will be stored on password protected computers at the University of Liverpool. Your participation will not affect your medical care.

Only the research team will be able to see the information will collect on you. This includes the audio recordings.

With your permission, we would want to tell your GP about your taking part. We would also need to tell your GP if the health professional giving your course or our researcher becomes worried about your health. However, we would talk about this with you first.

The Seizure First Aid Training course is given to groups of about 10 people with epilepsy and their family and friends. Because of this, we cannot promise that other participants will not share information about one another outside of the group. To lower the chances of this happening, we will get all participants to sign a form. This will say that they agree that anything they hear about other participants should not be talked about outside of the group. The health professional giving the course will remind participants of this at the start.

10. What if something goes wrong?

The University of Liverpool has insurance cover just in case you experience a problem from taking part. If you are worried about anything to do with the study, you should contact the research team. Their details are at the end of this sheet.

11. What will happen to the results of the study?

The results from this study will be used to see if any changes to the Seizure First Aid Training course are needed. They might also be published. You will not be identified in any publication. If you would like to have a copy of the published results, you can ask for one by contacting the study team.

All information generated by this study, including the transcriptions from the focus groups, will be held on password secured computers at the University of Liverpool offices. In line with the university's policy, data will be archived at the University of Liverpool for of at least 10 years, longer if judged to be of historical significance. After this period the data will be destroyed.

12. Who is funding and organising the study?

The study is funded by the National Institute for Health Research. The study is being done by the Institute of Psychology, Health and Society, The Whelan Building, University of Liverpool, L69 3GL. The lead researcher is Dr Adam Noble.

13. Who has reviewed the study?

This study has been reviewed and approved by National Research Ethics Service Committee North West - Liverpool East (Reference: 15/NW/0225).

14. Contact for further information:

Should you need further information about the study you can contact the research team at any time:

XXXXXXXX

You will be given a copy of this information sheet and a signed copy of your consent form to keep.

Appendix 4 Topic guide for interviews with health-care professional representatives (part A)

***Reminder of context of study for interviewer*:**

Many visits to hospital emergency departments for epilepsy are clinically unnecessary. This is because they are by people with known, rather than new epilepsy, who have experienced an uncomplicated seizure. Research by our group indicates people with established epilepsy often attend hospital emergency departments for these seizures because they and their significant others (SOs) can lack confidence managing seizures. They say they want more information, are unsure as to what the effects of seizures are, do not know when medical attention is required, and some fear death. To better support these people, we are developing a seizure first aid training course for patients who frequently visit emergency departments, and their family and friends. The course will be adapted from an existing seizure management training course that has been delivered on a small scale by the Epilepsy Society.

Tools:

To help the interview process, take a copy of the course materials that were sent to the interviewee. The table of 8 topics covered may be a useful aide memoire for interviewees. The interviewee is also encouraged to bring any notes with them to the interview.

Areas to be covered by the interview with health professional/ user group stakeholders:

- Briefly, what is their area/ work/ career background?
- How are they involved in supporting people with epilepsy?
- What were their thoughts on the idea of the course?
- How successful/ unsuccessful do they think the course will be in improving patients and SOs seizure management skills and confidence? Any particular groups for which is likely to be most or least useful?
- What did they think from the course was most likely/ least likely to help patients make fewer clinically unnecessary ED visits?
- Are there any new things that they think the course needs to cover so that it is as helpful as possible? If so, what and how?

Specific areas to be explored here if not covered spontaneously:

- Some patients may hold disproportionate fears concerning the effects of seizures on the brain and the possibility of death. Does the interviewee think some course time should be given to the topic of what the effects of seizures are and the risks of events, such as status epilepticus and SUDEP? If so, what information do they think the course should provide and how?

- Does the interviewee think evidence on the high proportion of unnecessary ED visits for epilepsy should be explicitly presented to participants?

- Does the interviewee think some course time should be given to allow participants to discuss fears of unconsciousness/death in themselves and SOs; and seizure management?

- Participants might not be aware of emergency seizure medication and may also have incorrect beliefs about them. Does the interviewee think some course time should be given to the topic of emergency medication? If so, what information should be relayed and how?

- Some ED visits occur because the person is alone, has an uncomplicated seizure in a public place, and a bystander calls for an ambulance. Does the interviewee think some course time be given to the topic of how patients and families can help ambulance crews manage seizures in the community when appropriate, rather than having to transport the patient to ED? If so, what information or strategies do you think the course should provide patients with and how?

- Are there any things that they think should be removed from the course? If so, what and why?

- To accommodate that additional aspect/s, whilst keep the course length roughly the same, what you do they think could be removed and why?

- Are there any things currently covered by the course that they think should be changed? If so, what and how?

- What did they think about the way the course is delivered? (Group sizes, setting, educational facilitator background, capacity etc.)

- Do they have any thoughts on how the course will be received by PWE who frequently visit ED?

- Are there any barriers to participating and/or using information and training that they identify?

- Do they have any thoughts on how the course will be received by the family members and friends who attend the course?

One specific area to be explored here if not covered spontaneously - Does the interviewee think some course time should be given to how patients can best discuss their epilepsy and first-aid with friends and colleagues not on the course? If so, what information or strategies do you think the course should provide patients with and how?

- Did they identify any inaccuracies in the medical information that was presented? If so, what/ where?

- If the course were ultimately found to be effective, how do they think it could be best rolled out within the NHS? (e.g., identifying who needs it; how often courses should be provided; who pays for it) What would be the barriers and facilitators be?

Close:

- Any other questions or comments participant wishes to make
- Thank you for your time

Appendix 5 Topic guide for focus groups with service user representatives (part A)

Introduction:

- Introduce self and project role
- Well once again I would like to thank you all for taking the time to be here with us today.
- As I mentioned previously we are now interested in finding out about your views about today's training. Your comments and suggestions for change are important to us as we want to use those ideas to help us improve the content and presentation of this training.
- Before we start this discussion I just want to mention a couple of important points:
    - The discussion will work best if everyone feels comfortable to share their opinion and sometimes personal experiences. It is important that we agree from the start that any personal details people speak about during this session are respected by us all and kept confidential by not sharing any personal information about anybody else outside of this room. Does this sound okay to everyone? ...Thank you
    - Please note this FG is being audio recorded for the purpose of data collection. The recording will be transcribed and I will use the findings from this discussion to inform the further development of this training package
    - Can I just confirm that everyone has signed a consent form? … you will receive a copy of this form to keep
    - Please feel free to speak openly – there are no right or wrong answers. However it would be useful if when making a comment you could say whether you are speaking as a PWE/SO. This will help me to understand which perspective your response is coming from.
    - Any questions before we begin?

Ice-breaker - General Overview:

Right, so let's get started

- **As you may already know there are lots of different types of epilepsy and everyone is individual. This probably meant that some of things we talked about today may have been important to some of you, while some things may not. Thinking about your impressions overall then:**

    - How well was today's session organised overall?

EXPLORE,

    - What did you particularly appreciate and/or enjoy about the session? *(prompts)*
        - Content
        - Presentation
        - Timeframe *(including start time and duration)*
        - Venue *(including access and facilities*)

EXPLORE,

- What changes could we introduce to improve the session? *(prompts)*
  - Content
  - Presentation
  - Timeframe *(including start time and duration)*
  - Venue *(including access and facilities*)

Use previous discussion as the platform to explore follow-on questions:

- **Today's course was designed to give you information about epilepsy first aid:**
  - In your opinion how well did the taught aspects of the session meet:
    - This aim / What could we have done differently
    - Your own expectations / What would you like to see changed
    - We also tried to provide people with epilepsy and those who support them with a practical view of how to manage seizures, including what to do and what not to when seizures occur:
    - In your opinion how good were the explanation of topics provided in the session
    - Was enough time given to these explanations
    - Was enough time given to the practical demonstrations (recovery position)
    - What could we have done differently

- **In the future, we want everyone who takes part in these sessions to contribute as much as possible as we believe this will make what is being said more meaningful for the participants. With this in mind:**

  - How comfortable did you feel to:
    - Ask questions about the topics covered
    - To participate in the practical tasks in the session

(prompts to explore in turn/ in depth)

- Kindness Questionnaire
- Quiz
- What to do/what not to do task
- Recovery demonstration/practice

- In your opinion Does group size/mix, promote/hinder interaction
  - Was the group size/mix of PWE/SOs appropriate:
    - Yes – why?/No – why?

- **This training session, its format and resources were informed by broader seizure management training that is currently offered by the Epilepsy Society. In your opinion:**
    - How well *(or not)* do you think the session title reflects the:
        - The session aims
        - The session content
- **Thinking specifically about the content of the session, in your opinion:**
    - Where the key message(s) from today's session easy to identify?
    - Was the amount of material covered was about right?
    - Was there anything that was unclear or could have been better explained?
    - Was there anything you wanted to be included that wasn't?
        - If so what was it and why was this important?
- **If you have had an opportunity to look at the additional information provided today:**
    - How relevant to the session do you consider them to be?
    - What additional information, not provided would you have liked to have been included?
- **I would now like to hear your opinions about how the session was delivered today:**
    - Was the session leader considered to be knowledgeable / provide quality instruction?
    - How well did the session leader develop a good rapport with those taking part?
    - Was class participation and interaction encouraged sufficiently / too much
    - Where the teaching and learning methods used stimulating / interesting?
    - How good was the balance between the session leader talking, the group work and the discussion?
    - Was adequate provided for questions and discussion?
    - Overall, how well organised was the session?

CLOSE

- Are there any other comments anyone would like to make about any aspect of today's session?
- THANKYOU

Appendix 6 Search criteria employed at the different recruitment sites to identify potentially suitable persons attending emergency departments for epilepsy

ED site		
1	**2**	**3**
Identify those people who in the free-text box 'presenting complaint' are recorded as having visited the ED for a: • 'fit' • 'epilepsy' • 'convulsion' • 'seizure' Identify those people admitted as an emergency from an ED to a ward with any of the following primary or secondary ICD-10 diagnoses: • 'G40 Epilepsy' • 'G41 Status epilepticus' • 'G83.8 Other specified paralytic syndromes' • 'R56.8 Other and unspecified convulsions'	Identify those people who in the free-text box 'reason for visit' or 'presenting complaint' are recorded as having visited the ED for: • 'fit' • 'epilep' • 'convuls' • 'seiz' Identify those people admitted as an emergency from an ED to a ward with any of the following primary or secondary ICD-10 diagnoses: • 'G40 Epilepsy' • 'G41 Status epilepticus' • 'G83.8 Other specified paralytic syndromes' • 'R56.8 Other and unspecified convulsions'	Identify those people who attended the ED and were given any of the following presenting complaint/ discharge diagnosis profiles: • 'AE20 AEPRC Fit' AND '02 AEDIG Contusion/abrasion' • 'AE20 AEPRC Fit' AND '04 AEDIG Head injury' • 'AE20 AEPRC Fit' AND '05 AEDIG Dislocation' • 'AE20 AEPRC Fit' AND '06 AEDIG Sprain/ligament injury' • 'AE20 AEPRC Fit' AND '07 AEDIG Muscle/tendon injury' • 'AE20 AEPRC Fit' AND '10 AEDIG Burns and scalds' • 'AE20 AEPRC Fit' AND '15 AEDIG Near Drowning' • 'AE20 AEPRC Fit' AND '33 AEDIG Facio-maxillary conditions' • 'AE20 AEPRC Fit' AND '38 AEDIG Diagnosis not classifiable' • '241 AEDIG Epilepsy' Identify those people admitted as an emergency from an ED to a ward with any of the following primary or secondary ICD-10 diagnoses: • 'G40 Epilepsy' • 'G41 Status epilepticus' • 'G83.8 Other specified paralytic syndromes' • 'R56.8 Other and unspecified convulsions'

ICD-10, *International Statistical Classification of Diseases and Related Health Problems*, Tenth Revision.

Appendix 7 Participant information sheet for patients in the pilot randomised controlled trial (project part B)

[INSERT TRUST LOGO]

PATIENT PARTICPANT INFORMATION SHEET

Study title: Research offering Seizure First Aid Training to people with epilepsy and their family and friends: A pilot trial (REC reference no: 5/NW/0225)

1. Invitation paragraph

You are being asked to take part in a research study. Before you decide whether you want to take part, it is important for you to know why the research is being done and what it will involve. Please read this information sheet carefully. If you wish to you can talk about it with your friends and relatives. Ask us if there is anything you do not understand or if you want more information. You can take time to decide whether you want to take part.

2. What is the reason for the study?

People with epilepsy need to know what to do when a seizure happens. They also need to be able to tell others what to do. This is also true for the friends and family of people with epilepsy. To feel confident to do these things, some people with epilepsy and family members have said they need more information about epilepsy and seizure first aid. They said they want to know more about the effects of seizures, how to deal with different types and know when they do and do not need emergency medical help. Therefore, together with the Epilepsy Society, we have made a short course on seizure first aid that people with epilepsy and their family and friends can go on. The course is called Seizure First Aid Training.

Ambulance staff, neurologists, nurses and emergency medicine doctors have helped us decide what information the course should give. The course takes 3 hours to do and people with epilepsy take it together with a family member or friend. It is a group based course so there are other people with epilepsy and their family and friends at the course. Our study is looking to see how helpful the Seizure First Aid Training course is. We want to know whether it helps people with epilepsy and their family and friends get the information they want and whether it makes them more confident managing seizures. We need to know this so the NHS can decide whether it should offer the course.

3. What type of study is it that you are doing?

The type of study we are doing is called a pilot randomised trial. In this sort of study, people taking part are put into one of two groups at random by a computer. The first group is called Group A and the second Group B. People who are put in Group A get the Seizure First Aid Training course straightaway and people in Group B continue to receive their normal medical care. The health of the people in the two groups is then compared to see if the Seizure First Aid Training was helpful or not.

After the two groups' health has been compared, people in Group B then get to go on a Seizure First Aid Training course if they want it. At the moment we do not know if the Seizure First Aid Training course is any more helpful

than the normal care people already receive from the NHS. This means a randomised trial is the most exact and fair way to see how helpful the course is. Each year thousands of people take part in randomised trials.

4. Why am I being asked to take part?

We are looking for people with epilepsy to take part in our study with a family member or friend. To take part in our study, people with epilepsy need to be aged 16 or over. They must have been diagnosed with epilepsy for 1 or more years and be prescribed anti-epileptic medication. They also need to have visited a hospital emergency department for epilepsy two or more times in the last 12 months. The person can have any type of epilepsy and their seizures can be of any severity. However, people cannot take part in the study if they experience non-epileptic seizures. The Seizure First Aid Training course is given in English. This means people can also only take part if they can speak, read and understand English well. You are being invited to take part because we believe you fit the above description.

5. Do I have to take part?

No. It is up to you. Even if you decide to take part, you are still free to change your mind at any time. You would not need to give a reason. A decision to not take part will not affect your medical care. No new information would be collected on you. However, any information that had already been collected would be kept.

6. What will happen to me if I take part?

If you want to take part, our researcher will arrange to see you at a time and place that is convenient for you. They could meet you at your home or our university offices. You will also be asked to choose a family member or friend to take part in the study with you. At the appointment, the researcher will explain the study to you and your family member or friend and answer any questions you have. You will be given this information sheet to keep and each asked to sign a consent form. You will then be asked to each fill in a questionnaire. It will ask your health, quality of life and how you manage seizures. The researcher will be on hand to help you if needed. The appointment will last about one hour. After the appointment, the researcher will use a computer programme to put you into either Group A or Group B. The group you are put in will decide when you and your family member or friend gets to go on the Seizure First Aid Training. You will not be able to choose which group you are put in and we will not make the decision ourselves. We will let you know which group you have been put in.

7. What will happen to me if I am put into Group A?

If you are put into Group A you will be asked to go on a Seizure First Aid Training course about a month after you signed the consent form. You will still continue to take your medications and see your doctors and nurses as normal.

After going on the course you will be asked to fill in a short questionnaire about your health three times. The first time will be three months after you joined the study. The researcher will telephone you and ask you the questions. It should take about 10 minutes. The second time will be six months after you joined the study. On

this occasion you will be sent the questionnaire in the post and asked to post it back to us when you have finished it. It should take you about 30 minutes to do.

The final time you will be asked to fill in the questionnaire will be about twelve months after you joined the study. You will do it during a face-to-face appointment with our researcher. This appointment will last about one hour and happen at a time and place that is convenient for you.

8. What will happen to me if I am put into Group B?

If you are put into Group B you will not get to go on the Seizure First Aid Training course straightway. Instead, you will continue to receive you normal medical care for the next 12 months and be asked to fill in a questionnaire on your health three times. The first time will be three months after you first filled it in. The researcher will telephone you and ask you the questions. It should take about 10 minutes. The second time will be six months after you first filled it in. On this occasion you will be sent the questionnaire in the post and asked to post it back to us when you have finished it. It should take you about 30 minutes to do.

The final time you will be asked to fill in the questionnaire will be about twelve months after you first filled it in. You will do it during a face-to-face appointment with our researcher. This appointment will last about one hour and happen at a time and place that is convenient for you. You will be able to go on a Seizure First Aid Training course after everyone in the study has completed their final questionnaire. This should mean your course will typically take place about six months after you filled in your final questionnaire.

9. Where and how will the Seizure First Aid Training courses be run?

The courses will be run on weekdays at a hospital near to your home. For the course, you will need to go to the hospital just once. The courses will typically run from [INSERT TIME] until [INSERT TIME], with breaks included. The research team will speak with you to find a course that is convenient for you to go to.

Each course will be given by a specially trained health professional from the charity, the Epilepsy Society. These people are typically nurses and will be able to help should a seizure happen. About 10 people with epilepsy and their family and friends will be at each of the courses. During the course, the health professional will give lots of information about epilepsy and show some video clips. They will talk about things people with epilepsy and their family and friends have said they want to know more about. This includes giving information on:

- How common epilepsy is.
- Its causes and some myths about epilepsy.
- The tests doctors use to diagnose it.
- The different types of seizures and their effects.

- How to deal with different seizures, including when to call an ambulance and how to help paramedics help you.
- How to improve your confidence and tell others what to do to if a person with epilepsy has a seizure.

At the course, you can ask questions. If you want to, you can share your experiences with the other people taking the course. Everyone taking the course is given an information pack to keep. It includes all the things talked about on the course. It also gives the details of support organisations. If you agree, we will audio-record the Seizure First Aid Training course sessions. We want to do this to have a record how well the course was run by the health professional. If illness means you can only go to part of the course, we can arrange for you to finish the course on another day.

10. How long would I be involved in the study?

If you are put into Group A you will be in the study for about one year. If you are in Group B you will typically be involved with the study for about 18 months.

11. Expenses

We do not expect you will have any expenses from taking part in our study. If needed, we can pay for a taxi to take you and your family member or friend to and from the course. We will also provide refreshments for you. All participants will receive a £10 shopping voucher for each of the questionnaires they do by post or in person. This is to thank them for their time and effort. Therefore, each person who takes part in our study can get up to £30. If you decide to take time off work to go on the course, we will not be able to pay you or your employer.

12. Are there any benefits in taking part?

We hope you and your family member or friend will get helpful information on epilepsy and learn some things that may increase your confidence to deal with seizures. However, this cannot be guaranteed. The information we get from the study may help us better support people with epilepsy in the future.

13. Are there any risks in taking part?

There are no known disadvantages or risks of taking part. Taking part in the study will not change the care you get for epilepsy. Your medicines will stay the same and you will see your usual doctors and nurses as normal. The Seizure First Aid Training course and some of the questionnaires that we will ask you will involve thinking about your epilepsy and feelings. For some people, this may be upsetting. You can stop taking part in the course or doing the questionnaire at any time. This would not affect your medical care in any way.

If taking part in the course or answering the questionnaires makes you worried about your feelings, you can talk to your GP. You can also ask the health professional giving your course for advice. However, they would not be able to refer you to any NHS service themselves.

14. Will my taking part in this study be kept confidential?

Yes. All the information we collect on you during the study will be kept confidential. Only the research team will be able to see the information. This includes the audio recordings. Anything that we publish or pass on will have your name and address and any personal information removed so that you cannot be identified. All information will be stored on password protected computers at the University of Liverpool. Your participation will not affect your medical care.

With your permission, we would want to tell your GP/ hospital specialist about your taking part. We would also need to speak with them and possibly access your medical records if the health professional giving your course or our researcher becomes worried about your wellbeing. However, we would talk about this with you first.

The Seizure First Aid Training course is given to groups of about 10 people with epilepsy and their family and friends. Because of this, we cannot promise that other participants will not share information about one another outside of the group. To lower the chances of this happening, we will get all participants to sign a form. This will say that they agree that anything they hear about other participants should not be talked about outside of the group. The health professional giving the course will remind participants of this.

As part of the project we would like to see if being in the study helps you become more confident to deal with seizures. One way we would like to find this out is by seeing if your use of hospital emergency departments changes. Information on when you have visited hospital emergency departments is already stored by the Health and Social Care Information Centre. They are a public body, sponsored by the Department of Health. With your agreement, we would like to see information held by the Health and Social Care Information Centre on your visits to hospital emergency departments. To do this, we would send the Health and Social Care Information Centre your NHS number and ask them for information on how many times you used hospital emergency departments in the 12 months before coming into our study and then how many times you went whilst you are in the study. All information that will be sent between the Health and Social Care Information Centre and us would be done using secure methods.

15. What happens when the study stops?

You continue to receive your normal medical care.

16. What if something goes wrong?

The University of Liverpool has insurance cover just in case you experience a problem from taking part in the study. If you are worried about anything to do with the study, you should contact the research team. Their details are at the end of this sheet.

17. What will happen to the results of the study?

The results from this study will be published in scientific journals. You will not be identified in any publication. If you want a copy of the published results, you can ask for one by contacting the study team. All information generated by this study will be held on password secured computers at the University of Liverpool offices. In line with the university's policy, data will be archived at the University of Liverpool for of at least 10 years, longer if judged to be of historical significance. After this period the data will be destroyed.

18. Who is funding and organising the study?

The study is funded by the National Institute for Health Research. The study is being done by the Institute of Psychology, Health and Society, The Whelan Building, University of Liverpool, L69 3GL. The lead researcher is Dr Adam Noble.

19. Who has reviewed the study?

This study has been reviewed and approved by National Research Ethics Service Committee North West - Liverpool East (Reference: 15/NW/0225).

20. Contact for further information:

Should you need further information about the study you can contact the research team at any time:

XXXXXXXX

Email: Seizure_First_Aid_project@liv.ac.uk

You will be given a copy of this information sheet and a signed copy of your consent form to keep.

Thank you!

Appendix 8 Full details of secondary outcome measures

Quality of life (patients only; baseline, 6 months and 12 months)

Quality of life was measured using the epilepsy-specific quality of life measure QOLIE-31-P.[184] This asks participants to reflect on how they felt over the past 4 weeks. It has seven subscales that reflect the aspects of living that can be affected by epilepsy (emotional well-being, energy fatigue, cognitive functioning, seizure worry, medication effects, social functioning and overall quality of life). Scored according to guidelines, a participant's total score ranges from 0 to 100, with higher scores indicating better overall perceived quality of life. The QOLIE-31-P varies from the original version of the tool[166] in that at the end of each subscale there is one additional item that asks the participant to rate the degree of 'distress' caused by that particular topic.

Burden (significant others only; baseline, 6 months and 12 months)

No epilepsy-specific measure is available to measure so-called 'caregiver burden' in the target population. Therefore, Zarit caregiver burden scores[170] were used to capture the impact of informal caring on the patient participant's designated SO. Its 22 items evaluate the effect of a condition on quality of life, difficulty in social and family relationships, psychological suffering, shame, guilt and financial difficulty. It is the most widely used, standardised, validated scale and has previously been used in epilepsy (Stavem *et al.*[231]).

Psychological distress (patients and significant others; baseline and 12 months)

The 14-item HADS[167,168] was used to measure self-reported distress in patients and SOs. It is a reliable, valid scale widely used in UK epilepsy research. Anxiety and depression scores are grouped into symptom categories: 'normal' (0–7), 'suggestive of anxiety/depression' (8–10) and 'probable anxiety/depression' (11–21).[232]

Felt stigma (patients only; baseline and 12 months)

Jacoby's 3-item Stigma Scale of Epilepsy with revised 4-point scoring[14,62,233] measured the extent to which patient participants felt that they are stigmatised because of their epilepsy. Response options include a four-point Likert scale: 'not at all' (0), 'yes, maybe' (1), 'yes, probably' (2) and 'yes, definitely' (3). A total score of 0 is classified as 'does not feel stigmatised' while total scores of 1–6 are classified as 'mildly to moderately stigmatised' and total scores of 7–9 are classified as 'highly stigmatised'. The scale's internal consistency (Cronbach's $\alpha = 0.85$) is good.[14]

Fear of seizures (patients and significant others; baseline and 12 months)

Both patients and SOs completed five items from the fears subscale of the 60-item Epilepsy Knowledge and Management questionnaire.[163] They focus on knowledge about seizures and on fears of death or brain damage. The five items have previously been used in isolation.[234]

Confidence managing seizures/epilepsy (patients and significant others; baseline, 6 months and 12 months)

The epilepsy-specific Wagner 6-item Mastery Scale[61] was used to measure patient participants' perception of epilepsy and its treatment and the extent to which they felt able to control these. This measure is able to distinguish between groups of PWE with differing levels of severity. It has adequate internal consistency (Cronbach's $\alpha = 0.7$) and test–retest reliability.[235] SOs completed the 6-item Condition Management subscale from the Parents Response to Child Illness Scale,[186] which has been shown to have good internal consistency.[165] SOs respond to each item using a 5-point scale.

Knowledge of what to do when faced with a seizure (patient and significant others; baseline and 12 months)

Both patients and SOs completed a measure assessing their knowledge of what to do when faced with a seizure. The standardised questions come from Martiniuk *et al.*'s Thinking About Epilepsy questionnaire.[164]

Seizure control (patients only; baseline, 6 months and 12 months)

At baseline (T0), patients were asked to complete Thapar's seizure frequency scale[169] for the prior 12 months. At 6- (T2) and 12-month (T3) follow-up, patient participants were asked for the number of seizures (of any type) that they had experienced since the last assessment and the date of the first and most recent seizure (if applicable) since last assessment. To assist patients to be able to provide this information they were offered a seizure diary at baseline (T0) and instructed on how to complete it.

Health economics (patients only; baseline and 12 months)

The Client Service Receipt Inventory[171] enabled measurement of patient participants' health service use (including use of ambulance services, regardless of whether or not transfer to ED happened), informal care (including work time lost by SOs), benefits received and employment status during the 12 months prior to baseline (T0) and at 12 months (T3). The 5-item EQ-5D,[172] already shown to be valid in PWE,[153] was also used.

Feedback on participation (patients and significant others and 12 months)

To capture patient and SOs feedback on their experience of taking part in the trial, including randomisation, we asked both parties to complete three questions at their final assessment. These were (1) 'If time suddenly went backward, and you had to do it all over again, would you agree to participate in the Seizure First Aid Training trial?' (options: 'definitely yes', 'probably yes', 'probably no', 'definitely no' and 'not sure', plus a free-text field to explain the response), (2) 'Please tell us if there was anything about the Seizure First Aid Training Trial that you think could have been done better' (options: free-text response) and (3) 'Please tell us if there was anything about the Seizure First Aid Training Trial, or your experience of joining the trial, that you think was particularly good' (options: free-text response). The questions are based on those used to explore participants' experience of participating in Morgan *et al.*'s Magpie trial.[236]

Appendix 9 Serious adverse event protocol

Event

We defined a SAE – adapting the definition in Medicines for Human Use (Clinical Trials) Regulations 2004[237] – as an adverse event that:

- resulted in death
- was life-threatening (subject at immediate risk of death, e.g. status epilepticus)
- resulted in a seizure that led to hospital admission for ≥ 24 hours
- resulted in emergency attendance or hospital admission for reason other than seizure
- resulted in persistent or significant disability or incapacity
- was otherwise considered medically significant.

'Life-threatening' in the context of 'serious' refers to an event in which the patient is at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe. Hospitalisations for a pre-existing condition, including elective procedures that had not worsened, do not constitute a SAE. Prolongation of hospital stay owing to social factors, for example geographical location of the participant's home, which prevented discharge is also not considered a SAE.

Given the characteristics of the subject population being studied, the following events are expected in this study population and will not be recorded as part of the SAE monitoring process:

- Epileptic seizures with or without injury.
- Emergency or urgent medical attention. This includes a visit to a hospital ED lasting < 24 hours, attending an NHS out-of-hours primary care service, telephoning for an ambulance, telephoning NHS 111, seeking/having an urgent/fast-tracked appointment with a usual care provider (GP or specialist) or other registered health-care professional (e.g. a pharmacist).
- Side effects of antiepileptic drug.
- Diagnosis of a comorbid psychiatric condition.

A delegated medically qualified person in the team (AM or LR) will assess each unexpected SAE. This person will consider information on the temporal and physical relationship between the event and possible causes and assess whether the event was related or unrelated to the patient's participation in the study. Further details on the process follow.

Monitoring

As part of this trial, patient participants will not receive additional medical reviews. There is also no 'live' system that can be used to track SAEs such as emergency admissions, and usual care providers are not systematically informed of them. Therefore, to monitor SAEs the research team will liaise with patients themselves. A standardised form will be completed as part of the CRF at 3 months (T1, by telephone), 6 months (T2, by telephone) and 12 months (T3, during a face-to-face appointment) post randomisation to collect information on patient participants' experience of unexpected SAEs.

In each instance, a maximum of three attempts will be made to contact the patient participant by telephone (including trying to contact them via their informal carer if they are taking part with one). Should the patient not be contactable a letter will be sent the patient's GP asking them to inform the research team if the patient is no longer alive and of the circumstances of their death.

Given the characteristics of the subject population being studied the potential adverse events expected in this study population are as follows:

- Epileptic seizures with or without injury.
- Emergency or urgent medical attention. This includes a visit to a hospital ED lasting < 24 hours, attending an NHS out-of-hours primary care service, telephoning for a ambulance, telephoning NHS 111, seeking/having an urgent/fast-tracked appointment with a usual care provider (GP or specialist) or other registered health-care professional (e.g. a pharmacist).
- Side effects of antiepileptic drug.
- Diagnosis of a comorbid psychiatric condition.

Although they will be captured as outcomes of the trial, they will not be recorded as part of the SAE monitoring process.

Causality

A delegated, medically qualified person in the team will assess each unexpected SAE. This person will consider information on the temporal and physical relationship between the event and possible causes and assess whether the event was related or unrelated to the patient's participation in the study. In doing this, they will use the definitions in the table below.

To complete their assessment, the research team may need to obtain medical records, such as contacting a hospital where a patient was admitted as an emergency. For the following reasons a window of 10 days will be allowed for a SAE to be reviewed by the medic: information on adverse events will have been collected by research workers during concentrated follow-up periods, there will be only one delegated medical assessor and assessment may depend on the timeliness of response from hospitals for historically distant admissions.

Definitions of causality for serious adverse event

Term	Description
Unrelated	There is no evidence of any causal relationship. There is an alternative cause for the SAE
Unlikely	There is little evidence to suggest that there is a causal relationship (e.g. the event did not occur within a reasonable time after receipt of the intervention). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatment)
Possibly	There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after receipt of the intervention). However, the influence of other factors may have contributed to the event (e.g. the participants clinical condition, other concomitant treatment)
Probably	There is evidence to suggest a causal relationship and the influence of other factors is unlikely
Almost certainly	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out

Reporting

The main research ethics committee (REC) approving the study and the sponsor will be informed within 15 days of the team becoming aware of any SAE that in the opinion of the medical reviewers is both unexpected (that is, the type of event is not listed in the protocol as an expected occurrence) and

judged to be 'possibly', 'probably' or 'almost certainly' related to participation in the study (that is, it resulted from administration of any of the research procedures, including the intervention).

Notifications will include the following details: date of the SAE, location, a description of the circumstances of the event and an assessment of the causal relationship to the SAFE intervention and the implications, if any, for the safety of study participants and how these will be addressed. Notifications made to the main REC shall be made using the National Research Ethics Service SAE reporting form for non-Clinical Trials of an Investigational Medicinal Product. A flowchart is given below to aid the determination of reporting requirements.

A log of all SAEs that are unexpected and which were judged to be related to participation in the study will also be reviewed by the Independent Trial Steering Committee and the implications for the study considered. This information will also be sent to the funder as part of the progress reports and the chief investigator will include details of the event in the annual progress report to the REC and a copy sent to the sponsor.

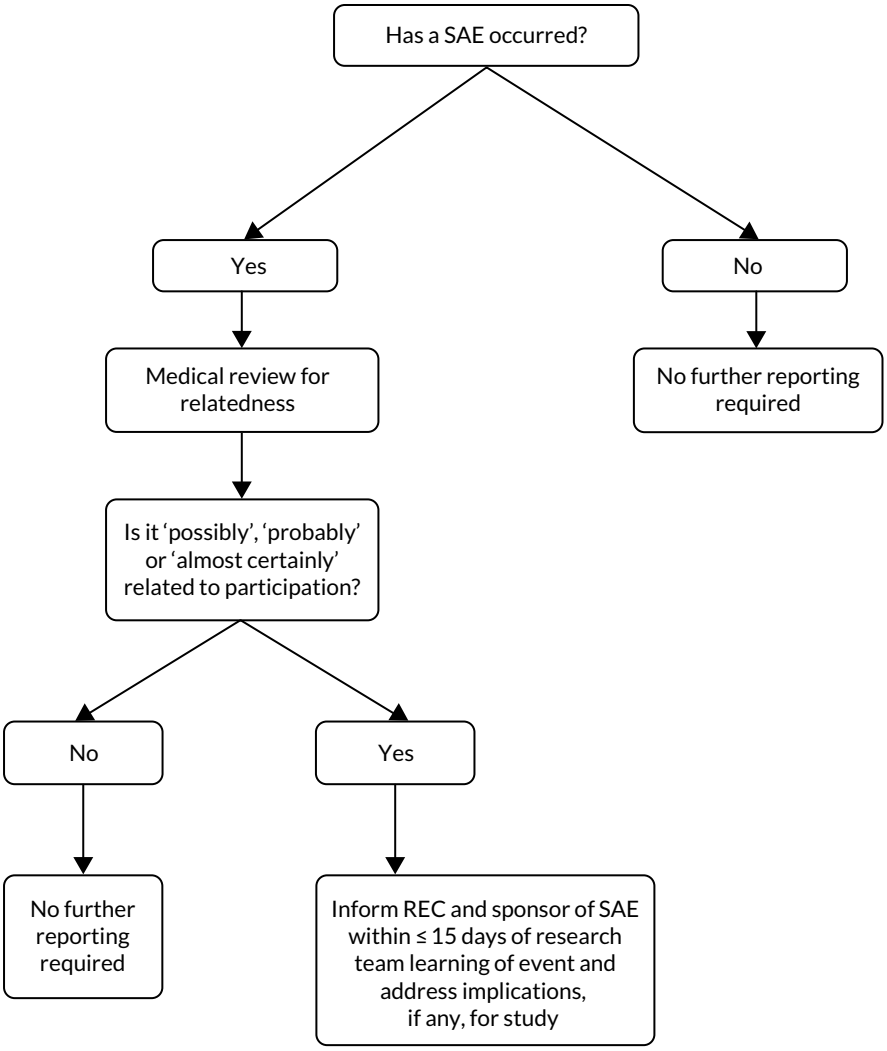
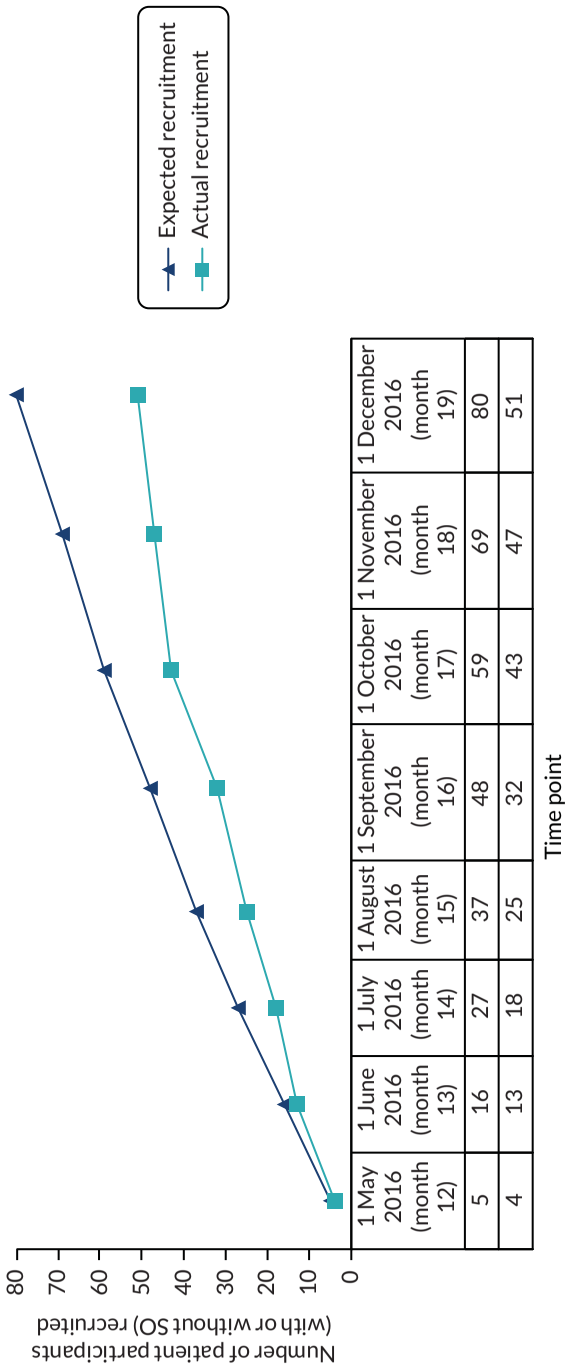


FIGURE Flowchart for determining of reporting requirements for SAEs.

Appendix 10 Cumulative, actual and expected recruitment (consented and randomised) to SAFE trial


Expected recruitment
Actual recruitment
Number of patient participants (with or without SO) recruited
0
10
20
30
40
50
60
70
80
Time point
1 May 2016 (month 12)
1 June 2016 (month 13)
1 July 2016 (month 14)
1 August 2016 (month 15)
1 September 2016 (month 16)
1 October 2016 (month 17)
1 November 2016 (month 18)
1 December 2016 (month 19)
5
16
27
37
48
59
69
80
4
13
18
25
32
43
47
51

Appendix 11 Reasons for withdrawal from the pilot randomised controlled trial

Reasons for withdrawal	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Patient participants withdrawing from the study	***(N = 1)***	***(N = 3)***	***(N = 4)***
Too busy	1 (100.0)	0 (0.0)	1 (25.0)
Not interested any more	0 (0.0)	1 (33.3)	1 (25.0)
Other: moved away to work	0 (0.0)	1 (33.3)	1 (25.0)
Other: wife has cancer	0 (0.0)	1 (33.3)	1 (25.0)
SO participants withdrawing from the study	***(N = 1)***	***(N = 4)***	***(N = 5)***
Too ill	0 (0.0)	1 (25.0)	1 (20.0)
Not interested any more	0 (0.0)	1 (25.0)	1 (20.0)
Other: moved away to work	0 (0.0)	1 (25.0)	1 (20.0)
Other: no longer friends with person with epilepsy	0 (0.0)	1 (25.0)	1 (20.0)
Reason missing	1 (100.0)	0 (0.0)	1 (20.0)

Appendix 12 Milestones in securing data from NHS Digital

	Project milestone		Milestone in obtaining data from NHS Digital	
Period	**Date**	**Note**	**Date**	**Note**
Pre trial	1 July 2015	Project officially starts		
	1 August 2015	Intervention development starts		
			28 September 2015	Received feedback on draft participant information sheets and consent form for trial to ensure compliance
Trial period	19 May 2016	First trial participant randomised		
			11 October 2017	Participated in NHS Digital training
			18 October 2017	Registered as new user of application system
			7 November 2017	Delays experienced. Access to application form granted after chasing
	December 2017	Final 12-month follow-up completed		
Post trial			16 February 2018	Application submitted to NHS Digital
			28 February 2018	Teleconference with NHS Digital. Provisional opinion given that only minor changes required and likely time frame for receipt of data 1.5 months
			7 March 2018	Received written feedback from NHS Digital after chasing on minor changes required
			22 March 2018	Revised application submitted
			3 April 2018	NHS Digital submitted new query (1) to applicants requesting additional information (applicants respond 3 April 2018)
			26 April 2018	NHS Digital submitted new query (2) to applicants requesting additional information (applicants respond 26 April 2018)
			30 April 2018	NHS Digital submitted new query (3) to applicants requesting additional information (applicants respond 30 April 2018)

Period	Project milestone		Milestone in obtaining data from NHS Digital	
	Date	Note	Date	Note
			5 May 2018	NHS Digital submitted new query (4) to applicants requesting additional information (applicants respond 5 May 2018)
			10 May 2018	NHS Digital submitted new query (5) to applicants requesting additional information (in the light of General Data Protection Regulation introduced in May 2018) (applicants respond 11 May 2018)
			30 May 2018	NHS Digital submitted new query (6) to applicants requesting additional information (in the light of General Data Protection Regulation introduced in May 2018) (applicants respond 30 May 2018)
			30 May 2018	NHS Digital submitted new query (7) to applicants requesting additional information (applicants respond 30 May 2018)
			15 June 2018	NHS Digital confirmed that data approvals owner will review revised application
			27 June 2018	NHS Digital submitted new query (8) to applicants requesting additional information and request revisions to trial website (in the light of General Data Protection Regulation introduced in May 2018) (applicants respond 28 June 2018)
			2 July 2018	NHS Digital submitted new query (9) to applicants requesting additional information (applicants 2 July 2018)
			6 July 2018	NHS Digital notified applicants that data approval owner has rejected application primarily because of 'concerns [over] whether this pilot would yield findings that were statistically valuable to achieve the stated aims given the small numbers'
			10 July 2018	Secured confirmation of right to appeal and process
			20 July 2018	Applicants submitted letter of appeal

	Project milestone		Milestone in obtaining data from NHS Digital	
Period	**Date**	**Note**	**Date**	**Note**
			25 July 2018	Appeal accepted by NHS Digital
			15 August 2018	NHS Digital submitted new query (10) to applicants following IGARD committee's review of application (applicants respond 16 August 2018)
			16 August 2018	Teleconference with NHS Digital data production team
			04 September 2018	NHS Digital sent data-sharing agreement to applicants
			10 September 2018	NHS Digital confirmed receipt of completed data-sharing agreement
			25 September 2018	Applicants securely transferred patient participants' details to NHS Digital
			31 September 2018	NHS Digital released data to applicants

IGARD, Independent Group Advising on the Release of Data.

Appendix 13 Completeness of secondary outcome measures by assessment point, tool and participant type

Number of questions of study assessment tool completed by patient participants at each time point

Number of questions of study assessment tool completed at each time point	Treatment arm, *n* (%)		
	SAFE plus TAU	TAU	Total, *n* (%)
Baseline (T0)	***(N = 26)***	***(N = 25)***	***(N = 51)***
QOLIE-31-P[184]			
33	0 (0.0)	1 (4.0)	1 (2.0)
35	2 (7.7)	2 (8.0)	4 (7.8)
36	1 (3.8)	6 (24.0)	7 (13.7)
37 (maximum)	23 (88.5)	16 (64.0)	39 (76.5)
[a]HADS[167,168]			
7	1 (3.8)	0 (0.0)	1 (2.0)
13	2 (7.7)	1 (4.0)	3 (5.9)
14 (maximum)	23 (88.5)	24 (96.0)	47 (92.2)
Stigma Scale of Epilepsy[62]			
0	1 (3.8)	1 (4.0)	2 (3.9)
2	1 (3.8)	0 (0.0)	1 (2.0)
3 (maximum)	24 (92.4)	24 (96.0)	48 (94.1)
[b]Client Service Receipt Inventory[171]			
2	1 (3.8)	0 (0.0)	1 (2.0)
4	1 (3.8)	0 (0.0)	1 (2.0)
5	5 (19.2)	8 (32.0)	13 (25.5)
6 (maximum)	19 (73.2)	17 (68.0)	36 (70.5)
EQ-5D[172]			
5	5 (19.2)	0 (0.0)	5 (9.8)
6 (maximum)	21 (80.8)	25 (100.0)	46 (90.2)
Wagner 6-item Mastery Scale[61]			
1	0 (0.0)	1 (4.0)	1 (2.0)
3	0 (0.0)	1 (4.0.)	1 (2.0)
5	0 (0.0)	2 (8.0)	2 (3.9)
6 (maximum)	26 (100.0)	21 (84.0)	47 (92.1)

Number of questions of study assessment tool completed at each time point	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Epilepsy Knowledge and Management Questionnaire:[163] fear of seizures subscale[163]			
0	3 (11.6)	2 (8.0)	5 (9.8)
1	1 (3.8)	1 (4.0)	2 (3.9)
2	1 (3.8)	5 (20.0)	6 (11.8)
3	1 (3.8)	4 (16.0)	5 (9.8)
4	4 (15.4)	4 (16.0)	8 (15.7)
5 (maximum)	16 (61.6)	9 (36.0)	25 (49.0)
6 months (T2)	***(N = 26)***	***(N = 25)***	***(N = 51)***
QOLIE-31-P[184]			
0	4 (15.4)	8 (32.0)[c]	12 (23.5)[c]
16	1 (3.8)	0 (0.0)	1 (2.0)
34	0 (0.0)	1 (4.0)	1 (2.0)
35	0 (0.0)	2 (8.0)	2 (3.9)
36	5 (19.2)	2 (8.0)	7 (13.7)
37 (maximum)	16 (61.6)	12 (48.0)	28 (54.9)
Wagner 6-item Mastery Scale[61]			
0	4 (15.4)	8 (32.0)[c]	12 (23.5)[c]
2	1 (3.8)	0 (0.0)	1 (2.0)
5	0 (0.0)	2 (4.0)	2 (3.9)
6 (maximum)	21 (80.8)	15 (60.0)	36 (70.6)
12 months (T3)	***(N = 26)***	***(N = 25)***	***(N = 51)***
QOLIE-31-P[184]			
0	7 (26.9)[d]	8 (32.0)[d]	15 (29.4)[d]
1	1 (3.8)	0 (0.0)	1 (2.0)
31	0 (0.0)	1 (4.0)	1 (2.0)
35	1 (3.8)	4 (16.0)	5 (9.8)
36	7 (26.9)	4 (16.0)	11 (21.6)
37 (maximum)	10 (38.5)	8 (32.0)	18 (35.3)
[a]HADS[167,168]			
0	8 (30.8)[d]	8 (32.0)[d]	16 (31.4)[d]
14 (maximum)	18 (69.2)	17 (68.0)	35 (68.6)
Stigma Scale of Epilepsy[62]			
0	8 (30.8)[d]	8 (32.0)[d]	16 (31.4)[d]
3 (maximum)	18 (69.2)	17 (68.0)	35 (68.6)

Number of questions of study assessment tool completed at each time point	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
[b]Client Service Receipt Inventory[171]			
0	8 (30.8)[d]	8 (32.0)[d]	16 (31.4)[d]
3	0 (0.0)	1 (4.0)	1 (2.0)
4	1 (3.8)	1 (4.0)	2 (3.9)
5	4 (15.4)	5 (20.0)	9 (17.7)
6 (maximum)	13 (50.0)	10 (40.0)	23 (45.0)
EQ-5D[172]			
0	8 (30.8)[d]	8 (32.0)[d]	16 (31.4)[d]
6	18 (69.2)	17 (68.0)	35 (68.6)
Wagner 6-item Mastery Scale[61]			
0	8 (30.8)[d]	8 (32.0)[d]	16 (31.4)[d]
5	0 (0.0)	1 (4.0)	1 (2.0)
6	18 (69.2)	16 (64.0)	34 (66.6)
Epilepsy Knowledge and Management Questionnaire:[163] fear of seizures subscale[163]			
0	10 (38.5)[d]	8 (32.0)[d]	18 (35.3)[d]
1	1 (3.8)	0 (0.0)	1 (2.0)
2	1 (3.8)	0 (0.0)	1 (2.0)
3	1 (3.8)	7 (28.0)	8 (15.7)
4	5 (19.2)	5 (20.0)	10 (19.6)
5 (maximum)	8 (30.9)	5 (20.0)	13 (25.5)

a Completeness of the whole HADS scale (both anxiety and depression subscales).
b Only six mandatory questions counted. Conditional questions (e.g. 'if yes, then') were not counted towards total completion.
c Including two patient participants from the TAU arm who had withdrawn by the 6-month (T2) visit.
d Including four patient participants (three from the TAU arm and one from the SAFE plus TAU arm) who had withdrawn by the 12-month (T3) visit.

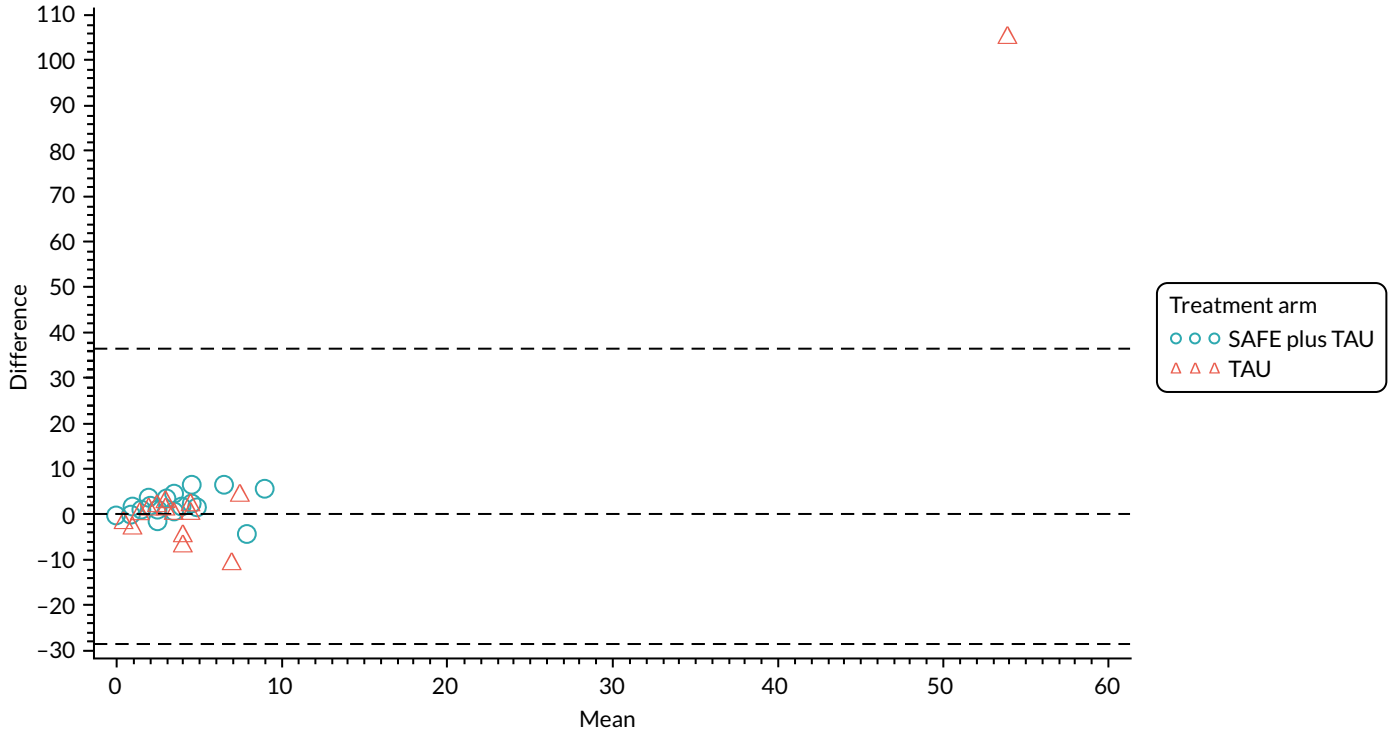
Number of questions of study assessment tool completed by significant other participants at each time point

Number of questions of study assessment tool completed at each time point	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Baseline (T0)	***(N = 18)***	***(N = 19)***	***(N = 37)***
Zarit caregiver burden[170]			
16	0 (0.0)	1 (5.3)	1 (2.7)
21	1 (5.6)	1 (5.3)	2 (5.4)
22 (maximum)	17 (94.4)	17 (89.5)	34 (91.9)
[a]HADS[167,168]			
13	1 (5.6)	1 (5.3)	2 (5.4)
14 (maximum)	17 (94.4)	18 (94.7)	35 (94.6)

Number of questions of study assessment tool completed at each time point	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Parent Response to Child Illness scale[186]			
6 (maximum)	18 (100.0)	19 (100.0)	37 (100.0)
Epilepsy Knowledge and Management Questionnaire:[163] fear of seizures subscale[163]			
0	2 (11.1)	2 (10.5)	4 (10.8)
1	2 (11.1)	2 (10.5)	4 (10.8)
2	1 (5.6)	3 (15.8)	4 (10.8)
3	1 (5.6)	2 (10.5)	3 (8.1)
4	6 (33.3)	6 (31.6)	12 (32.4)
5 (maximum)	6 (33.3)	4 (21.1)	10 (27.0)
6 months (T2)	***(N = 18)***	***(N = 19)***	***(N = 37)***
Zarit caregiver burden[170]			
0	2 (11.1)[b]	9 (47.4)[b]	11 (29.7)[b]
10	0 (0.0)	1 (5.3)	1 (2.7)
21	1 (5.6)	1 (5.3)	2 (5.4)
22 (maximum)	15 (83.4)	8 (42.0)	23 (62.2)
Parent Response to Child Illness scale[186]			
0	2 (11.1)[b]	10 (52.6)[b]	12 (32.4)[b]
6 (maximum)	16 (88.9)	9 (47.4)	25 (67.6)
12 months (T3)	***(N = 18)***	***(N = 19)***	***(N = 37)***
Zarit caregiver burden[170]			
0	7 (38.9)[c]	9 (47.4)[c]	16 (43.2)[c]
22 (maximum)	11 (61.1)	10 (52.6)	21 (56.8)
[a]HADS[167,168]			
0	7 (38.9)[c]	9 (47.4)[c]	16 (43.2)[c]
14 (maximum)	11 (61.1)	10 (52.6)	21 (56.8)
Parent Response to Child Illness scale[186]			
0	7 (38.9)[c]	9 (47.4)[c]	16 (43.2)[c]
6 (maximum)	11 (61.1)	10 (52.6)	21 (56.8)
Epilepsy Knowledge and Management Questionnaire:[163] fear of seizures subscale[163]			
0	7 (38.9)[c]	10 (52.7)[c]	17 (46.0)[c]
1	1 (5.6)	0 (0.0)	1 (2.7)
2	2 (11.1)	2 (10.5)	4 (10.8)
3	2 (11.1)	3 (15.8)	5 (13.5)
4	0 (0.0)	2 (10.5)	2 (5.4)
5 (maximum)	6 (33.3)	2 (10.5)	8 (21.6)

a Completeness of the whole HADS scale (both anxiety and depression subscales).
b Including four SO participants (one in the SAFE plus TAU arm and three in the TAU arm) who had withdrawn by the 6-month (T2) visit.
c Including four SO participants (one in the SAFE plus TAU arm and four in the TAU arm) who had withdrawn by the 12-month (T3) visit.

Appendix 14 Bland–Altman plot of agreement between self-reported and Hospital Episode Statistics data on emergency department visits at baseline, without any exclusions


Difference
Mean
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
−30
0
10
20
30
40
50
60
Treatment arm
SAFE plus TAU
TAU

Appendix 15 Demographic characteristics of significant other participants

Demographic characteristic	Treatment arm		Total
	SAFE plus TAU	TAU	
Relationship with patient participant*, n *(%)	***(N = 18)***	***(N = 19)***	***(N = 37)***
Parent	4 (22.2)	4 (21.1)	8 (21.6)
Son/daughter	2 (11.1)	4 (21.1)	6 (16.2)
Grandparent	0 (0.0)	0 (0.0)	0 (0.0)
Spouse/partner	9 (50.0)	7 (36.8)	16 (43.2)
Sibling	1 (5.6)	0 (0.0)	1 (2.7)
Cousin, aunt/uncle	0 (0.0)	0 (0.0)	0 (0.0)
Niece/nephew	0 (0.0)	1 (5.3)	1 (2.7)
Friend	2 (11.1)	3 (15.8)	5 (13.5)
Other	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Co-habitation with patient participant*, n *(%)	***(N = 18)***	***(N = 19)***	***(N = 37)***
Yes	14 (77.8)	14 (73.4)	28 (75.7)
No	4 (22.2)	5 (26.3)	9 (24.3)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Contact with patient participant (days per week)*, n *(%)	***(N = 18)***	***(N = 19)***	***(N = 37)***
0	0 (0.0)	0 (0.0)	0 (0.0)
1	1 (5.6)	0 (0.0)	1 (2.7)
2	0 (0.0)	1 (5.3)	1 (2.7)
3	0 (0.0)	2 (10.5)	2 (5.4)
4	0 (0.0)	0 (0.0)	0 (0.0)
5	0 (0.0)	0 (0.0)	0 (0.0)
6	0 (0.0)	0 (0.0)	0 (0.0)
7 (every day)	17 (94.4)	16 (84.2)	33 (89.2)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Sex*, n *(%)	***(N = 18)***	***(N = 19)***	***(N = 37)***
Male	6 (33.3)	9 (47.4)	15 (40.5)
Female	12 (67.7)	10 (52.6)	22 (59.5)
Missing	0 (0.0)	0 (0.0)	0 (0.0)

Demographic characteristic	Treatment arm		Total
	SAFE plus TAU	TAU	
Age (years) at consent into the trial			
n (%)	17 (94.4)	19 (100.0)	36 (94.6)
Mean, years	41.3	44.9	43.2
SD, years	18.66	15.69	17.01
Minimum, years	17.8	18.1	17.8
Median, years	43.5	49.7	48.0
Maximum, years	79.7	71.5	79.7
Missing, *n* (%)	1 (5.6)	0 (0.0)	1 (2.7)
Ethnicity,* n *(%)	***(N = 18)***	***(N = 19)***	***(N = 37)***
White	18 (100.0)	18 (94.5)	36 (97.3)
Asian/Asian British	0 (0.0)	0 (0.0)	0 (0.0)
Black/African/Caribbean/black British	0 (0.0)	0 (0.0)	0 (0.0)
Mixed/multiple	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	1 (5.3)	1 (2.7)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Significant medical history,* n *(%)	***(N = 18)***	***(N = 19)***	***(N = 37)***
No, none	13 (72.2)	12 (63.2)	25 (67.6)
Yes, a medical condition	5 (27.8)	6 (31.6)	11 (29.7)
Yes, a psychiatric condition	0 (0.0)	0 (0.0)	0 (0.0)
Yes, both medical and psychiatric conditions	0 (0.0)	1 (5.3)	1 (2.7)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
Education,* n *(%)	***(N = 18)***	***(N = 19)***	***(N = 37)***
O levels/GCSEs/Level 1 or 2 NVQ	9 (50.0)	14 (73.7)	23 (62.2)
A levels/Level 3 NVQ	4 (22.2)	2 (10.5)	6 (16.2)
University degree/graduate certificate or diploma	5 (27.8)	3 (15.8)	8 (21.6)
Postgraduate university degree (e.g. PGCE, MSc, MA, PhD)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)	0 (0.0)

A level, Advanced level; MA, Master of Arts; MSc, Master of Science; PGCE, Postgraduate Certificate in Education; PhD, Doctor of Philosophy.

Appendix 16 Adherence ratings for each checklist item and module

Module	Mean adherence rating for module across courses (SD; range)	Item	Mean adherence rating for item across courses (range)
Orientation and behaviour change optimisation	1.98 (0.08; 1.50–2.00)	1. Welcome	1.92 (1.50–2.00)
		2. Goals of this course	2.00 (2.00–2.00)
		3. What would you like from today?	2.00 (2.00–2.00)
		4. True or false?	2.00 (2.00–2.00)
		5. Taking on information (kindness questionnaire)	2.00 (2.00–2.00)
Basic epilepsy and first aid knowledge	1.86 (0.37; 0.00–2.00)	6. Epilepsy, seizures and how the brain works	2.00 (2.00–2.00)
		7. First aid for convulsive seizures exercise	2.00 (2.00–2.00)
		8. What can you do to help someone during a seizure?	2.00 (2.00–2.00)
		9. What not to do during a seizure	2.00 (2.00–2.00)
		10. What to do after the seizure has stopped	2.00 (2.00–2.00)
		11. Questions or comments	2.00 (2.00–2.00)
		12. Post-seizure states	1.64 (1.00–2.00)
		13. Injuries	1.07 (0.00–2.00)
		14. When to call an ambulance?	1.92 (1.50–2.00)
		15. Questions or comments	2.00 (2.00–2.00)
Recovery position	1.55 (0.78; 0.00–2.00)	16. Recovery position I	0.79 (0.00–2.00)
		17. Recovery position II	2.00 (2.00–2.00)
		18. Let's practise the recovery position	1.71 (0.00–2.00)
		19. Questions or comments	1.71 (0.00–2.00)
Informing others about epilepsy and how to help if seizures occur	1.95 (0.14; 1.50–2.00)	1. Who needs to know how to help?	1.93 (1.50–2.00)
		2. What they need to know and why	2.00 (2.00–2.00)
		3. How to get this information to them: family, friends and work colleagues	2.00 (2.00–2.00)
		4. How to get this information to them: members of the public and health workers	2.00 (2.00–2.00)
		5. Questions or comments	1.86 (1.50–2.00)

Module	Mean adherence rating for module across courses (SD; range)	Item	Mean adherence rating for item across courses (range)
Medical identification, seizure triggers and home safety	2.00 (0.00; 2.00–2.00)	6. Personal stories: introduction	2.00 (2.00–2.00)
		7. Ben's story	2.00 (2.00–2.00)
		8. How to change what happened to Ben	2.00 (2.00–2.00)
		9. Triggers	2.00 (2.00–2.00)
		10. Knowing your triggers	2.00 (2.00–2.00)
		11. Some ways of dealing with triggers	2.00 (2.00–2.00)
		12. Sandra's story	2.00 (2.00–2.00)
		13. How to change what happened to Sandra (warning signs; home safety)	2.00 (2.00–2.00)
Summary and consolidating learning	1.77 (0.50; 0.00–2.00)	14. Main points to remember if you have epilepsy	1.93 (1.50–2.00)
		15. Main points to remember if you know someone with epilepsy	2.00 (2.00–2.00)
		16. Sources of further information	1.57 (0.00–2.00)
		17. What's on the back table and accessing the study website	1.50 (0.00–2.00)
		18. Questions or comments	1.86 (1.00–2.00)

Appendix 17 Number of self-reported epilepsy-related emergency department visits

Number of epilepsy-related ED visits	Treatment arm		Total
	SAFE plus TAU	TAU	
During the 12 months prior to baseline (T0)			
n (%)	24 (92.3)	21 (84.0)	45 (88.2)
Mean	4.2	8.4	6.2
SD	2.91	22.75	15.63
Minimum[a]	0	0	0
Median	3.5	4.0	4.0
Maximum	12	107	107
Missing	2 (7.7)	4 (16.0)	6 (11.8)
During the 12 months following randomisation according to participant self-report			
n (%)	17 (65.4)	17 (68.0)	34 (67.7)
Mean	1.2	2.9	2.1
SD	1.60	5.55	4.11
Minimum	0	0	0
Median	0	1	1
Maximum	4	23	23
Missing	9 (34.6)	8 (32.0)	17 (33.3)
Change from baseline over 12 months following randomisation according to participant self-report[b]			
n (%)	16 (61.5)	14 (56.0)	30 (58.8)
Mean	−2.6	−0.3	−1.5
SD	2.83	6.17	4.75
Minimum	−10	−10	−10
Median	−2	−2	−2
Maximum	1	18	18
Missing	10 (38.5)	11 (44.0)	21 (41.2)

a Four participants reported no ED visits in the 12 months prior to baseline, even though the inclusion criteria for eligibility into the trial required at least two ED visits in the 12 months prior to baseline. This reflects inaccuracy and inconsistency in self-reporting.
b Calculated only for patient participants with a baseline and 12-month measure reported.

Appendix 18 Baseline scores of patient participants and significant other participants and change over follow-up period on secondary outcome measures

Quality of life

Total QOLIE-31-P score (patient participants with complete clinical research form data)

	Treatment arm		
Total QOLIE-31-P score[a]	**SAFE plus TAU**	**TAU**	**Total**
Baseline (T0)			
n (%)	23 (88.5)	16 (64.0)	39 (76.5)
Mean	51.2	44.1	48.3
SD	18.4	14.92	17.25
Minimum	17.7	17.1	17.1
Median	48.8	42.6	46.3
Maximum	78.7	79.5	79.5
Missing, *n* (%)	3 (11.5)	9 (36.0)	12 (23.5)
6 months (T2)			
n (%)	16 (61.5)	12 (48.0)	28 (54.9)
Mean	49.5	43.0	46.7
SD	21.86	10.46	17.92
Minimum	10.4	20.4	10.4
Median	50.2	45.1	47.7
Maximum	85.7	59.8	85.7
Missing, *n* (%)	10 (38.5)	13 (52.0)	23 (45.1)
12 months (T3)			
n (%)	10 (38.5)	8 (32.0)	18 (35.3)
Mean	47.6	42.9	45.5
SD	20.35	12.23	16.93
Minimum	9.7	23.8	9.7
Median	48.6	48.6	47.0
Maximum	72.9	57.0	72.9
Missing, *n* (%)	16 (61.5)	17 (68.0)	33 (64.7)
Change from baseline (T0) at 6 months (T2)[b]			
n (%)	14 (53.8)	8 (32.0)	22 (43.1)
Mean	−5.9	−0.7	−4.0
SD	13.81	8.57	12.20

Total QOLIE-31-P score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Minimum	−33.7	−12.0	−33.7
Median	−6.5	−1.8	−3.2
Maximum	18.7	12.9	18.7
Missing, *n* (%)	12 (46.2)	17 (68.0)	29 (56.9)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	10 (38.5)	6 (24.0)	16 (31.4)
Mean	0.8	−2.18	−0.3
SD	10.72	10.48	10.38
Minimum	−14.9	−19.5	−19.5
Median	1.0	−0.9	0.2
Maximum	20.5	12.9	20.5
Missing, *n* (%)	16 (61.5)	19 (76.0)	35 (68.6)

a Total QOLIE-31-P score ranges from 0 to 100; higher scores correspond to a better quality of life.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Total QOLIE-31-P score (patient participants with complete data following data imputation)

Total QOLIE-31-P score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	25 (96.2)	24 (96.0)	49 (96.1)
Mean	51.6	44.3	48.0
SD	18.63	16.38	17.77
Minimum	17.7	12.3	12.3
Median	48.8	42.6	46.3
Maximum	78.7	79.5	79.5
Missing, *n* (%)	1 (3.8)	1 (4.0)	2 (3.9)
6 months (T2)			
n (%)	21 (80.8)	14 (56.0)	35 (68.6)
Mean	47.8	42.6	45.7
SD	21.67	9.76	17.86
Minimum	10.4	20.4	10.4
Median	49.7	43.6	44.4
Maximum	85.7	59.8	85.7
Missing, *n* (%)	5 (19.2)	11 (44.0)	16 (31.4)
12 months (T3)			
n (%)	18 (69.2)	12 (48.0)	30 (58.8)
Mean	51.0	44.0	48.2
SD	20.43	11.72	17.58

Total QOLIE-31-P score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Minimum	9.7	23.8	9.7
Median	48.6	47.3	47.3
Maximum	82.8	57.0	82.8
Missing, *n* (%)	8 (30.8)	13 (52.0)	21 (41.2)
Change from baseline (T0) at 6 months (T2)[b]			
n (%)	20 (76.9)	13 (52.0)	33 (64.7)
Mean	−3.0	−0.8	−2.2
SD	13.16	9.07	11.61
Minimum	−33.7	−12.3	−33.7
Median	−2.4	−1.6	−1.6
Maximum	18.7	15.7	18.7
Missing, *n* (%)	6 (23.1)	12 (48.0)	18 (35.3)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	18 (69.2)	12 (48.0)	30 (58.9)
Mean	2.2	−1.9	0.6
SD	11.27	12.13	11.59
Minimum	−20.5	−22.7	−22.7
Median	2.1	−0.9	1.0
Maximum	20.5	18.6	20.5
Missing, *n* (%)	8 (30.8)	13 (52.0)	21 (41.2)

a Total QOLIE-31-P score ranges from 0 to 100; higher scores correspond to a better quality of life.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Caregiver burden

Total burden score (significant other participants with complete clinical research form data)

Total burden score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	17 (94.4)	17 (89.5)	34 (91.9)
Mean	15.8	20.6	18.2
SD	11.01	13.59	12.42
Minimum	0	0	0
Median	14.0	19.0	15.5
Maximum	45	45	45
Missing, *n* (%)	1 (5.6)	2 (10.5)	3 (8.1)

Total burden score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
6 months (T2)			
n (%)	15 (83.3)	8 (42.1)	23 (62.2)
Mean	19.7	22.7	20.7
SD	12.13	11.3	11.68
Minimum	0	13	0
Median	19	20	19
Maximum	42	48	48
Missing, *n* (%)	3 (16.7)	11 (57.9)	14 (37.8)
12 months (T3)			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	19.5	24.9	22.1
SD	16.24	15.83	15.88
Minimum	0	7	0
Median	15	20	18
Maximum	48	54	54
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)
Change from baseline (T0) at 6 months (T2)[b]			
n (%)	14 (77.8)	7 (36.8)	21 (56.8)
Mean	2.7	1.6	2.3
SD	7.01	6.21	6.62
Minimum	−9	−5	−9
Median	1	1	1
Maximum	20	12	20
Missing, *n* (%)	4 (22.2)	12 (63.2)	16 (43.2)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	10 (55.6)	9 (47.4)	19 (51.4)
Mean	1.4	0.8	1.1
SD	10.04	8.38	9.04
Minimum	−20	−12	−20
Median	0.5	2.0	1.0
Maximum	15	14	15
Missing, *n* (%)	8 (44.4)	10 (52.6)	18 (48.6)

a Total burden score ranges from 0 to 88; higher scores correspond to a greater level of burden.
b Calculated only for SO participants with a baseline and 12-month measurement reported.

Burden categories (significant other participants with complete clinical research form data)

Burden category	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Baseline (T0)			
Little or no burden	12 (66.7)	10 (52.7)	22 (59.5)
Mild to moderate burden	4 (22.2)	5 (26.3)	9 (24.3)
Moderate to severe burden	1 (5.6)	2 (10.5)	3 (8.1)
Severe burden	0 (0.0)	0 (0.0)	0 (0.0)
Missing	1 (5.6)	2 (10.5)	3 (8.1)
6 months (T2)			
Little or no burden	9 (50.0)	4 (21.1)	13 (35.1)
Mild to moderate burden	5 (27.7)	3 (15.8)	8 (21.6)
Moderate to severe burden	1 (5.6)	1 (5.3)	2 (5.4)
Severe burden	0 (0.0)	0 (0.0)	0 (0.0)
Missing	3 (16.7)	11 (57.8)	14 (37.8)
12 months (T3)			
Little or no burden	6 (33.3)	5 (26.3)	11 (29.7)
Mild to moderate burden	4 (22.2)	3 (15.8)	7 (18.9)
Moderate to severe burden	1 (5.6)	2 (10.5)	3 (8.1)
Severe burden	0 (0.0)	0 (0.0)	0 (0.0)
Missing	7 (38.9)	9 (47.4)	16 (43.2)

Total burden score (all significant other participants, including those with missing clinical research form data)

Total burden score[a]	Treatment arm		Total
	SAFE plus TAU	TAU	
Baseline (T0)			
n (%)	18 (100.0)	19 (100.0)	37 (100.0)
Mean	17.1	20.7	18.9
SD	12.00	13.03	12.51
Minimum	0	0	0
Median	14.5	19.0	16.0
Maximum	45	45	45
Missing, *n* (%)[b]	0 (0.0)	0 (0.0)	0 (0.0)
6 months (T2)			
n (%)	16 (88.9)	10 (52.6)	26 (70.3)
Mean	19.4	22.7	20.7
SD	11.78	9.98	11.04
Minimum	0	13	0

Total burden score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Median	19.0	22.0	19.5
Maximum	42	48	48
Missing, *n* (%)[b]	2 (11.1)	9 (47.4)	11 (29.7)
12 months (T3)			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	19.5	24.9	22.1
SD	16.24	15.83	15.88
Minimum	0	7	0
Median	15	20	18
Maximum	48	54	54
Missing, *n* (%)[b]	7 (38.9)	9 (47.4)	16 (43.2)
Change from baseline (T0) at 6 months (T2)[c]			
n (%)	16 (88.9)	10 (52.6)	26 (70.3)
Mean	1.4	2.0	1.7
SD	7.89	6.96	7.41
Minimum	−15	−7	−15
Median	0.0	1.5	0.5
Maximum	20	13	20
Missing, *n* (%)	2 (11.1)	9 (47.4)	11 (29.7)
Change from baseline (T0) at 12 months (T3)[c]			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	2.1	0.9	1.5
SD	9.79	7.91	8.74
Minimum	−20	−12	−20
Median	1	2	1
Maximum	15	14	15
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)

a Total burden score ranges from 0 to 88; higher scores correspond to a greater level of burden.
b Participants had no data recorded for the outcome.
c Calculated only for SO participants with a baseline and 12-month measurement reported.

Burden categories (all significant other participants, including those with missing clinical research form data)

Burden category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
Little or no burden	12 (67.7)	11 (57.9)	23 (62.2)
Mild to moderate burden	5 (27.8)	6 (31.6)	11 (29.7)
Moderate to severe burden	1 (5.6)	2 (10.5)	3 (8.1)
Severe burden	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)	0 (0.0)

Burden category	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
6 months (T2)			
Little or no burden	10 (55.6)	4 (21.1)	14 (37.8)
Mild to moderate burden	5 (27.8)	5 (26.3)	10 (27.0)
Moderate to severe burden	1 (5.6)	1 (5.3)	2 (5.4)
Severe burden	0 (0.0)	0 (0.0)	0 (0.0)
Missing	2 (11.1)	9 (47.4)	11 (29.7)
12 months (T3)			
Little or no burden	6 (33.3)	5 (26.3)	11 (29.7)
Mild to moderate burden	4 (22.2)	3 (15.8)	7 (18.9)
Moderate to severe burden	1 (5.6)	2 (10.5)	3 (8.1)
Severe burden	0 (0.0)	0 (0.0)	0 (0.0)
Missing	7 (38.9)	9 (47.4)	16 (43.2)

Distress

Total anxiety score (patient participants with complete clinical research form data)

Total anxiety score[a]	Treatment arm		Total
	SAFE plus TAU	TAU	
Baseline (T0)			
n (%)	25 (96.2)	25 (100.0)	50 (98.0)
Mean	10.2	10.4	10.3
SD	5.22	4.54	4.84
Minimum	2	0	0
Median	11	11	11
Maximum	20	18	20
Missing, *n* (%)	1 (3.8)	0 (0.0)	1 (2.0)
12 months (T3)			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	10.8	10.6	10.7
SD	5.49	3.18	4.46
Minimum	3	5	3
Median	10.5	10.0	10.0
Maximum	19	16	19
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	0.2	−0.6	−0.2

Total anxiety score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
SD	3.91	3.26	3.58
Minimum	−7	−7	−7
Median	−0.5	−1	−1
Maximum	13	6	13.0
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)

a Total anxiety score ranges from 0 to 21; higher scores correspond to higher levels of anxiety.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Anxiety categories (patient participants with complete clinical research form data)

Anxiety category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
Normal range	9 (34.6)	5 (20.0)	14 (27.5)
Suggestive of anxiety	3 (11.5)	7 (28.0)	10 (19.6)
Probable anxiety	13 (50.0)	13 (52.0)	26 (50.9)
Missing	1 (3.8)	0 (0.0)	1 (2.0)
12 months (T3)			
Normal range	6 (33.3)	2 (8.0)	8 (15.6)
Suggestive of anxiety	3 (16.7)	8 (32.0)	11 (21.6)
Probable anxiety	9 (50.0)	7 (28.0)	16 (31.4)
Missing	8 (30.8)	8 (32.0)	16 (31.4)

Total anxiety score (patient participants with complete data following data imputation)

Total anxiety score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	25 (96.2)	25 (100.0)	50 (98.0)
Mean	10.2	10.4	10.3
SD	5.22	4.54	4.84
Minimum	2	0	0
Median	11	11	11
Maximum	20	18	20
Missing, *n* (%)	1 (3.8)	0 (0.0)	1 (2.0)
12 months (T3)			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	10.8	10.6	10.7
SD	5.49	3.18	4.46

Total anxiety score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Minimum	3	5	3
Median	10.5	10.0	10.0
Maximum	19	16	19
Missing, *n* (%)	8 (30.8)	8 (40.0)	16 (31.4)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	0.2	−0.6	−0.2
SD	3.91	3.26	3.58
Minimum	−7	−7	−7
Median	−0.5	−1	−1
Maximum	13	6	13.0
Missing, *n* (%)	8 (30.8)	8 (40.0)	16 (31.4)

a Total anxiety score ranges from 0 to 21; higher scores correspond to higher levels of anxiety.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Anxiety categories (patient participants with complete data following data imputation)

Anxiety category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
Normal range	9 (34.6)	5 (20.0)	14 (27.5)
Suggestive of anxiety	3 (11.5)	7 (28.0)	10 (19.6)
Probable anxiety	13 (50.0)	13 (52.0)	26 (50.9)
Missing	1 (3.8)	0 (0.0)	1 (2.0)
12 months (T3)			
Normal range	6 (33.3)	2 (8.0)	8 (15.6)
Suggestive of anxiety	3 (16.7)	8 (32.0)	11 (21.6)
Probable anxiety	9 (50.0)	7 (28.0)	16 (31.4)
Missing	8 (30.8)	8 (32.0)	16 (31.4)

Total depression score (patient participants with complete clinical research form data)

Total depression score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	23 (88.5)	24 (96.0)	47 (92.2)
Mean	6.6	8.7	7.7
SD	4.51	4.67	4.66
Minimum	0	0	0

Total depression score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Median	7.0	8.5	7
Maximum	17	19	19
Missing, *n* (%)	3 (11.5)	1 (4.0)	4 (7.8)
12 months (T3)			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	7.2	8.6	7.9
SD	4.07	3.46	3.80
Minimum	1	4	1
Median	7	9	8
Maximum	14	16	16
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)
12 months (T3)[b]			
n (%)	16 (61.5)	16 (64.0)	32 (62.7)
Mean	−0.5	0.1	−0.2
SD	1.97	2.90	2.46
Minimum	−3	−5	−5
Median	−0.5	1.0	0.0
Maximum	3	5	5
Missing, *n* (%)	10 (38.5)	9 (36.0)	19 (37.3)

a Total depression score ranges from 0 to 21; higher scores correspond to higher levels of depression.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Depression categories (patient participants with complete clinical research form data)

Depression category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
Normal range	14 (53.9)	10 (40.0)	24 (47.1)
Suggestive of depression	5 (19.2)	7 (28.0)	12 (23.5)
Probable depression	4 (15.4)	7 (28.0)	11 (21.6)
Missing	3 (11.5)	1 (4.0)	4 (7.8)
12 months (T3)			
Normal range	10 (38.4)	7 (28.0)	17 (33.3)
Suggestive of depression	4 (15.4)	4 (16.0)	8 (15.7)
Probable depression	4 (15.4)	6 (24.0)	10 (19.6)
Missing	8 (30.8)	8 (32.0)	16 (31.4)

Total depression score (patient participants with complete data following data imputation)

Total depression score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	25 (96.2)	25 (100.0)	50 (98.0)
Mean	6.7	8.6	7.6
SD	4.36	4.61	4.53
Minimum	0	0	0
Median	7	8	7.5
Maximum	17	19	19
Missing, *n* (%)	1 (3.8)	0 (0.0)	1 (2.0)
12 months (T3)			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	7.2	8.6	7.9
SD	4.07	3.46	3.80
Minimum	1	4	1
Median	7	9	8
Maximum	14	16	16
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	−0.2	0.5	0.1
SD	2.39	3.16	2.77
Minimum	−3.0	−5.0	−5.0
Median	−0.5	1.0	0.0
Maximum	5.8	6.2	6.2
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)

a Total depression score ranges from 0 to 21; higher scores correspond to higher levels of depression.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Depression categories (patient participants with complete data following data imputation)

Depression category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
Normal range	14 (53.8)	11 (44.0)	25 (49.0)
Suggestive of depression	7 (26.9)	7 (28.0)	14 (27.5)
Probable depression	4 (15.3)	7 (28.0)	11 (21.6)
Missing	1 (3.8)	0 (0.0)	1 (2.0)

Depression category	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
12 months (T3)			
Normal range	10 (38.4)	7 (28.0)	17 (33.3)
Suggestive of depression	4 (15.3)	4 (16.0)	8 (15.7)
Probable depression	4 (15.3)	6 (24.0)	10 (19.6)
Missing	8 (30.8)	8 (32.0)	16 (31.4)

Total anxiety score (significant other participants with complete clinical research form data)

Total anxiety score[a]	Treatment arm		Total
	SAFE plus TAU	TAU	
Baseline (T0)			
n (%)	17 (94.4)	18 (94.7)	35 (94.6)
Mean	8.4	7.9	8.1
SD	4.21	4.37	4.24
Minimum	2	0	0
Median	9	10	9
Maximum	15	14	15
Missing, *n* (%)	1 (5.6)	1 (5.3)	2 (5.4)
12 months (T3)			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	9.2	8.2	8.7
SD	5.15	2.39	4.01
Minimum	1	4	1
Median	9	9	9
Maximum	16	12	16
Missing, *n* (%)	7 (38.9)	9 (47.8)	16 (43.2)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	0.5	−0.5	0.0
SD	2.70	3.13	2.88
Minimum	−3	−5	−5
Median	1	−1.5	−1
Maximum	3	5	5
Missing, *n* (%)	7 (38.9)	9 (47.8)	16 (43.2)

a Total anxiety score ranges from 0 to 21; higher scores correspond to higher levels of anxiety.
b Calculated only for SO participants with a baseline and 12-month measurement reported.

Anxiety categories (significant other participants with complete clinical research form data)

Anxiety category	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Baseline (T0)			
Normal range	7 (38.9)	7 (36.8)	14 (37.8)
Suggestive of anxiety	4 (22.2)	3 (15.8)	7 (18.8)
Probable anxiety	6 (33.3)	8 (42.1)	14 (37.8)
Missing	1 (5.6)	1 (5.3)	2 (5.4)
12 months (T3)			
Normal range	4 (22.2)	4 (21.1)	8 (21.7)
Suggestive of anxiety	2 (11.1)	5 (26.3)	7 (18.9)
Probable anxiety	5 (27.8)	1 (5.3)	6 (16.2)
Missing	7 (38.9)	9 (47.8)	16 (43.2)

Total anxiety score (significant other participants with complete data following data imputation)

Total anxiety score[a]	Treatment arm		Total
	SAFE plus TAU	TAU	
Baseline (T0)			
n (%)	18 (100.0)	19 (100.0)	37 (100.0)
Mean	8.4	8.3	8.3
SD	4.09	4.47	4.23
Minimum	2	0.0	0.0
Median	9.0	10.0	9.3
Maximum	15	14	15
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
12 months (T3)			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	9.2	8.2	8.7
SD	5.15	2.39	4.01
Minimum	1	4	1
Median	9	9	9
Maximum	16	12	16
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	0.5	−0.5	0.0
SD	2.70	3.13	2.88

Total anxiety score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Minimum	−3	−5	−5
Median	1.0	−1.5	−1.0
Maximum	3	5	5
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)

a Total anxiety score ranges from 0 to 21; higher scores correspond to higher levels of anxiety.
b Calculated only for SO participants with a baseline and 12-month measurement reported.

Anxiety categories (significant other participants with complete data following data imputation)

Anxiety category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
Normal range	7 (38.9)	7 (36.8)	14 (37.8)
Suggestive of anxiety	5 (27.8)	3 (15.8)	8 (21.7)
Probable anxiety	6 (33.3)	9 (47.4)	15 (40.5)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
12 months (T3)			
Normal range	4 (22.2)	4 (21.1)	8 (21.7)
Suggestive of anxiety	2 (11.1)	5 (26.3)	7 (18.9)
Probable anxiety	5 (27.8)	1 (5.3)	6 (16.2)
Missing	7 (38.9)	9 (47.4)	16 (43.2)

Total depression score (significant other participants with complete clinical research form data)

Total depression score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	18 (100.0)	19 (100.0)	37 (100.0)
Mean	4.3	3.4	3.8
SD	4.40	2.65	3.59
Minimum	0	0	0
Median	2.5	3.0	3.0
Maximum	12	8	12
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
12 months (T3)			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	5.2	5.1	5.1
SD	3.60	3.60	3.51
Minimum	0	0	0

Total depression score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Median	5	5	5
Maximum	12	11	12
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)
Change from baseline at 12 months (T3)[b]			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	−0.4	1.3	0.4
SD	3.14	1.83	2.68
Minimum	−9	−1	−9
Median	0	1	1
Maximum	3	4	4
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)

a Total depression score ranges from 0 to 21; higher scores correspond to higher levels of depression.
b Calculated only for SO participants with a baseline and 12-month measurement reported.

Depression categories (significant other participants with complete clinical research form data)

Depression category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
Normal range	14 (77.8)	18 (94.7)	32 (86.5)
Suggestive of depression	1 (5.6)	1 (5.3)	2 (5.4)
Probable depression	3 (16.7)	0 (0.0)	3 (8.1)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
12 months (T3)			
Normal range	7 (38.9)	8 (42.1)	15 (40.6)
Suggestive of depression	3 (16.7)	1 (5.3)	4 (10.8)
Probable depression	1 (5.6)	1 (5.3)	2 (5.4)
Missing	7 (38.9)	9 (47.4)	16 (43.2)

Total depression score (significant other participants with complete data following data imputation)

Total depression score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	18 (100.0)	19 (100.0)	37 (100.0)
Mean	4.3	3.4	3.8
SD	4.40	2.65	3.59
Minimum	0	0	0

Total depression score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Median	2.5	3.0	3
Maximum	12	8	12
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
12 months (T3)			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	5.2	5.1	5.1
SD	3.60	3.60	3.51
Minimum	0	0	0
Median	5	5	5
Maximum	12	11	12
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	−0.4	1.3	0.4
SD	3.14	1.83	2.68
Minimum	−9	−1	−9
Median	0	1	1
Maximum	3	4	4
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)

a Total depression score ranges from 0 to 21; higher scores correspond to higher levels of depression.
b Calculated only for SO participants with a baseline and 12-month measurement reported.

Depression categories (significant other participants with complete data following data imputation)

Depression category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
Normal range	14 (77.8)	18 (94.7)	32 (86.5)
Suggestive of depression	1 (5.6)	1 (5.3)	2 (5.4)
Probable depression	3 (16.7)	0 (0.0)	3 (8.1)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
12 months (T3)			
Normal range	7 (38.9)	8 (42.1)	15 (40.6)
Suggestive of depression	3 (16.7)	1 (5.3)	4 (10.8)
Probable depression	1 (5.6)	1 (5.3)	2 (5.4)
Missing	7 (38.9)	9 (47.4)	16 (43.2)

Stigma

Total stigma score (patient participants with complete clinical research form data)

Total stigma score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	24 (92.3)	24 (96.0)	48 (94.1)
Mean	3.2	4.1	3.6
SD	2.45	3.26	2.89
Minimum	0	0	0
Median	3	3	3
Maximum	7	9	9
Missing, *n* (%)	2 (7.7)	1 (4.0)	3 (5.9)
12 months (T3)			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	3.2	3.9	3.5
SD	2.57	3.03	2.79
Minimum	0	0	0
Median	3.5	3.0	3.0
Maximum	8	9	9
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	17 (65.4)	17 (68.0)	34 (66.7)
Mean	−0.1	0.3	0.1
SD	2.30	1.79	2.04
Minimum	−6	−2	−6
Median	0	0	0
Maximum	4	4	4
Missing, *n* (%)	9 (34.6)	8 (32.0)	17 (33.3)

a Total stigma score ranges from 0 to 9; higher scores correspond to higher levels of stigma.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Stigma categories (patient participants with complete clinical research form data)

Stigma category	Treatment arm, *n* (%): SAFE plus TAU	Treatment arm, *n* (%): TAU	Total, *n* (%)
Baseline (T0)			
No stigma	4 (15.4)	3 (12.0)	7 (13.7)
Mildly to moderately stigmatised	13 (50.0)	13 (52.0)	26 (51.0)
Highly stigmatised	7 (26.9)	8 (32.0)	15 (29.4)
Missing	2 (7.7)	1 (4.0)	3 (5.9)

Stigma category	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
12 months (T3)			
No stigma	4 (15.4)	3 (12.0)	7 (13.7)
Mildly to moderately stigmatised	10 (38.4)	8 (32.0)	18 (35.3)
Highly stigmatised	4 (15.4)	6 (24.0)	10 (19.6)
Missing	8 (30.8)	8 (32.0)	16 (31.4)

Total stigma score (all patient participants, including those with missing clinical research form data)

Total stigma score[a]	Treatment arm		Total
	SAFE plus TAU	TAU	
Baseline (T0)			
n (%)	25 (96.2)	24 (96.0)	49 (96.8)
Mean	3.2	4.1	3.6
SD	2.41	3.26	2.87
Minimum	0	0	0
Median	3	3	3
Maximum	7	9	9
Missing, *n* (%)[b]	1 (3.8)	1 (4.0)	2 (3.9)
12 months (T3)			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	3.2	3.9	3.5
SD	2.57	3.03	2.79
Minimum	0	0	0
Median	3.5	3.0	3.0
Maximum	8	9	9
Missing, *n* (%)[b]	8 (30.8)	8 (32.0)	16 (31.4)
Change from baseline (T0) at 12 months (T3)[c]			
n (%)	17 (65.4)	17 (68.0)	34 (66.7)
Mean	−0.1	0.3	0.1
SD	2.30	1.79	2.04
Minimum	−6	−2	−6
Median	0	0	0
Maximum	4	4	4
Missing, *n* (%)	9 (34.6)	8 (32.0)	17 (33.3)

a Total stigma score ranges from 0 to 9; higher scores correspond to higher levels of stigma.
b Participants had no data recorded for the outcome.
c Calculated only for patient participants with a baseline and 12-month measurement reported.

Stigma categories (all patient participants, including those with missing clinical research form data)

Stigma category	Treatment arm, *n* (%)		Total, *n* (%)
	SAFE plus TAU	TAU	
Baseline (T0)			
No stigma	4 (15.4)	3 (12.0)	7 (13.7)
Mildly to moderately stigmatised	14 (53.9)	13 (52.0)	27 (52.9)
Highly stigmatised	7 (26.9)	8 (32.0)	15 (29.4)
Missing	1 (3.8)	1 (4.0)	2 (3.9)
12 months (T3)			
No stigma	4 (15.4)	3 (12.0)	7 (13.7)
Mildly to moderately stigmatised	10 (38.4)	8 (32.0)	18 (35.3)
Highly stigmatised	4 (15.4)	6 (24.0)	10 (19.6)
Missing	8 (30.8)	8 (32.0)	16 (31.4)

Fear of seizures

Total fear score (patient participants with complete clinical research form data)

Total fear score[a]	Treatment arm		Total
	SAFE plus TAU	TAU	
Baseline (T0)			
n (%)	16 (61.5)	9 (36.0)	25 (49.0)
Mean	16.4	17.6	16.8
SD	5.48	4.77	5.16
Minimum	6	8	6
Median	17	18	17
Maximum	24	25	25
Missing, *n* (%)	10 (38.5)	16 (64.0)	26 (51.0)
12 months (T3)			
n (%)	8 (30.8)	5 (20.0)	13 (25.5)
Mean	15.5	20.8	17.5
SD	5.32	2.49	5.07
Minimum	8	17	8
Median	16	21	18
Maximum	23	23	23
Missing, *n* (%)	18 (69.2)	20 (80.0)	38 (74.5)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	6 (23.1)	3 (12.0)	9 (17.6)
Mean	−1.5	2.0	−0.3
SD	2.66	1.00	2.78

Total fear score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Minimum	−6	1	−6
Median	−1.5	2.0	0.0
Maximum	2	3	3
Missing, *n* (%)	20 (76.9)	22 (88.0)	42 (82.4)

a Total fear score ranges from 5 to 30; higher scores correspond to greater levels of fear.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Total fear score (all patient participants, including those with missing clinical research form data)

Total fear score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	23 (88.5)	23 (92.0)	46 (90.2)
Mean	15.2	13.6	14.4
SD	5.32	5.80	5.56
Minimum	5	3[b]	3[b]
Median	16	14	14
Maximum	24	25	25
Missing, *n* (%)[c]	3 (11.5)	2 (8.0)	5 (9.8)
12 months (T3)			
n (%)	16 (61.5)	17 (68.0)	33 (64.7)
Mean	14.4	16.0	15.2
SD	4.88	4.15	4.52
Minimum	5	10	5
Median	15	16	16
Maximum	23	23	23
Missing, *n* (%)[c]	10 (38.5)	8 (32.0)	18 (35.3)
Change from baseline (T0) at 12 months (T3)[d]			
n (%)	15 (57.7)	17 (68.0)	32 (62.8)
Mean	0.6	1.5	1.1
SD	4.03	7.25	5.89
Minimum	−6	−10	−10
Median	0	1	0
Maximum	9	18	18
Missing, *n* (%)	11 (42.3)	8 (32.0)	19 (37.2)

a Total fear score ranges from 5 to 30; higher scores correspond to greater levels of fear.
b Minimum reported score less than minimum possible score of 5 owing to missing data treated as zeros.
c Participants had no data recorded for the outcome.
d Calculated only for patient participants with a baseline and 12-month measurement reported.

Total fear score (significant other participants with complete clinical research form data)

Total fear score[a]	Treatment arm		Total
	SAFE plus TAU	TAU	
Baseline (T0)			
n (%)	6 (33.3)	4 (21.1)	10 (27.0)
Mean	15.5	16.0	15.7
SD	3.45	3.92	3.43
Minimum	10	11	10
Median	15.5	16.5	15.5
Maximum	20	20	20
Missing, *n* (%)	12 (66.7)	21 (78.9)	27 (73.0)
12 months (T3)			
n (%)	6 (33.3)	2 (10.5)	8 (21.6)
Mean	20.7	22.5	21.1
SD	3.78	0.71	3.31
Minimum	16	22	16
Median	22.0	22.5	22.5
Maximum	24	23	24
Missing, *n* (%)	12 (67.7)	17 (89.5)	29 (78.4)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	3 (16.7)	0	3 (8.8)
Mean	6.7	NA[c]	6.7
SD	7.02	NA[c]	7.02
Minimum	0	NA[c]	0
Median	6	NA[c]	6.0
Maximum	14	NA[c]	14
Missing, *n* (%)	15 (83.3)	19 (100.0)	34 (91.2)

NA, not applicable.
a Total fear score ranges from 5 to 30; higher scores correspond to greater levels of fear.
b Calculated only for SO participants with a baseline and 12-month measurement reported.
c No SO participants in the TAU arm had complete CRF data at both baseline (T0) and at 12 months (T3); therefore, change in total fear score could not be calculated.

Total fear score (all significant other participants, including those with missing clinical research form data)

Total fear score[a]	Treatment arm		Total
	SAFE plus TAU	TAU	
Baseline (T0)			
n (%)	16 (88.9)	17 (89.5)	33 (89.2)
Mean	13.8	12.4	13.1
SD	4.83	5.10	4.95

Total fear score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Minimum	4[b]	1[b]	1[b]
Median	14.5	13.0	14.0
Maximum	20	20	20
Missing, *n* (%)[c]	2 (11.1)	2 (10.5)	4 (10.8)
12 months (T3)			
n (%)	11 (61.1)	9 (47.4)	20 (54.0)
Mean	15.6	16.0	15.8
SD	6.59	5.00	5.78
Minimum	5	9	5
Median	16	16	16
Maximum	24	23	24
Missing, *n* (%)[c]	7 (38.9)	10 (52.6)	17 (46.0)
Change from baseline (T0) at 12 months (T3)[d]			
n (%)	9 (50.0)	8 (42.1)	17 (45.9)
Mean	2.2	1.9	2.1
SD	5.40	4.76	4.96
Minimum	−4	−5	−5
Median	0.0	2.5	0.0
Maximum	14	7	14
Missing, *n* (%)	9 (50.0)	11 (57.9)	20 (54.1)

a Total fear score ranges from 5 to 30; higher scores correspond to greater levels of fear.
b Minimum reported score less than minimum possible score of 5 owing to missing data treated as zeros.
c Participants had no data recorded for the outcome.
d Calculated only for SO participants with a baseline and 12-month measurement reported.

Confidence in managing seizures/epilepsy

Total mastery score (patient participants with complete clinical research form data)

Total mastery score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	26 (100.0)	21 (84.0)	47 (92.3)
Mean	13.9	12.1	13.1
SD	2.86	2.95	3.00
Minimum	8	7	7
Median	14	12	13
Maximum	20	19	20
Missing, *n* (%)	0 (0.0)	4 (16.0)	4 (7.8)
6 months (T2)			
n (%)	21 (84.6)	15 (60.0)	36 (70.6)
Mean	12.7	11.7	12.3

Total mastery score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
SD	3.89	2.97	3.53
Minimum	7	6	6
Median	11	12	11
Maximum	21	17	21
Missing, *n* (%)	4 (15.4)	10 (40.0)	15 (29.4)
12 months (T3)			
n (%)	18 (69.2)	16 (64.0)	34 (66.7)
Mean	13.8	11.3	12.6
SD	3.47	2.60	3.29
Minimum	9	6	6
Median	13.5	12.0	12.0
Maximum	21	16	21
Missing, *n* (%)	8 (30.8)	9 (36.0)	17 (33.3)
Change from baseline (T0) at 6 months (T2)[b]			
n (%)	21 (80.8)	12 (48.0)	33 (64.7)
Mean	−0.7	−1.4	−0.9
SD	3.71	3.34	3.54
Minimum	−8	−8	−8
Median	−1	−2	−1
Maximum	8	4	8
Missing, *n* (%)	5 (19.2)	13 (52.0)	18 (35.3)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	18 (69.2)	14 (56.0)	32 (62.7)
Mean	0.2	−1.1	−0.4
SD	2.96	3.41	3.17
Minimum	−5	−9	−9
Median	0.5	−1.0	0.0
Maximum	6	3	6
Missing, *n* (%)	8 (30.8)	11 (44.0)	19 (37.3)

a Total mastery score ranges between 6 and 24; higher scores correspond to higher levels of mastery.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Total mastery score (all patient participants, including those with missing clinical research form data)

Total mastery score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	26 (100.0)	25 (100.0)	51 (100)
Mean	13.9	11.4	12.7
SD	2.86	3.50	3.40
Minimum	8	3[b]	3[b]

Total mastery score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Median	14	12	13
Maximum	20	19	20
Missing, *n* (%)[c]	0 (0.0)	0 (0.0)	0 (0.0)
6 months (T2)			
n (%)	22 (84.6)	17 (68.0)	39 (76.5)
Mean	12.3	11.4	11.9
SD	4.32	2.91	3.76
Minimum	3[d]	6	3[d]
Median	11	11	11
Maximum	21	17	21
Missing, *n* (%)[c]	4 (15.4)	8 (32.0)	12 (23.5)
12 months (T3)			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	13.8	11.5	12.7
SD	3.47	2.60	3.25
Minimum	9	6	6
Median	13.5	12.0	12.0
Maximum	21	16	21
Missing, *n* (%)[c]	8 (30.8)	8 (32.0)	16 (31.4)
Change from baseline (T0) at 6 months (T2)[c]			
n (%)	22 (84.6)	17 (68.0)	39 (76.5)
Mean	−1.2	−0.2	−0.8
SD	4.35	4.25	4.28
Minimum	−12	−8	−12
Median	−1	−1	−1
Maximum	8	11	11
Missing, *n* (%)	4 (15.4)	8 (32.0)	12 (23.5)
Change from baseline (T0) at 12 months (T3)[c]			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	0.2	−0.5	−0.2
SD	2.96	3.36	3.13
Minimum	−5	−9	−9
Median	0.5	0.0	0.0
Maximum	6	3	6
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)

a Total mastery score ranges between 6 and 24; higher scores correspond to higher levels of mastery.
b Calculated only for patient participants with a baseline and 12-month measurement reported.
c Participants had no data recorded for the outcome.
d Minimum reported score less than minimum possible score of 6 owing to missing data treated as zeros.

Total confidence score (significant other participants with complete clinical research form data)

Total confidence score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	18 (100.0)	19 (100.0)	37 (100.0)
Mean	3.5	3.8	3.6
SD	0.62	0.72	0.69
Minimum	2.0	2.3	2.0
Median	3.5	3.8	3.7
Maximum	4.5	5.0	5.0
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
6 months (T2)			
n (%)	16 (88.9)	9 (47.4)	25 (67.6)
Mean	4.2	3.9	4.1
SD	0.75	0.71	0.73
Minimum	2.7	2.8	2.7
Median	4.1	4.0	4.0
Maximum	5.0	4.8	5.0
Missing, *n* (%)	2 (11.1)	10 (52.6)	12 (32.4)
12 months (T3)			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	4.3	4.1	4.2
SD	0.57	0.99	0.78
Minimum	3.5	2.2	2.2
Median	4.2	4.7	4.3
Maximum	5.0	5.0	5.0
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)
Change from baseline (T0) at 6 months (T2)[b]			
n (%)	16 (88.9)	9 (47.4)	25 (67.6)
Mean	0.6	0.2	0.5
SD	0.70	0.32	0.61
Minimum	−0.8	−0.2	−0.8
Median	0.6	0.2	0.2
Maximum	1.7	0.8	1.7
Missing, *n* (%)	3 (11.1)	10 (52.6)	12 (32.4)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	0.7	0.3	0.5
SD	0.49	0.43	0.50
Minimum	0.0	−0.2	−0.2

Total confidence score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Median	0.7	0.3	0.5
Maximum	1.7	1.0	1.7
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)

a Total confidence score ranges between 1 and 5; higher scores correspond to higher levels of confidence.
b Calculated only for SO participants with a baseline and 12-month measurement reported.

Total confidence score (all significant other participants, including those with missing clinical research form data)

Total confidence score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	18 (100.0)	19 (100.0)	37 (100.0)
Mean	3.5	3.8	3.6
SD	0.62	0.72	0.69
Minimum	2.0	2.3	2.0
Median	3.5	3.8	3.7
Maximum	4.5	5.0	5.0
Missing, *n* (%)[b]	0 (0.0)	0 (0.0)	0 (0.0)
6 months (T2)			
n (%)	16 (88.9)	9 (47.4)	25 (67.6)
Mean	4.2	3.9	4.1
SD	0.75	0.71	0.73
Minimum	2.7	2.8	2.7
Median	4.1	4.0	4.0
Maximum	5.0	4.8	5.0
Missing, *n* (%)[b]	2 (11.1)	10 (52.6)	12 (32.4)
12 months (T3)			
n (%)	11 (61.1)	10 (52.6)	21 (56.6)
Mean	4.3	4.1	4.2
SD	0.57	0.99	0.78
Minimum	3.5	2.2	2.2
Median	4.2	4.7	4.3
Maximum	5.0	5.0	5.0
Missing, *n* (%)[b]	7 (38.9)	9 (47.4)	16 (43.24)
Change from baseline (T0) at 6 months (T2)[c]			
n (%)	16 (88.9)	9 (47.4)	25 (67.6)
Mean	0.6	0.2	0.5
SD	0.70	0.32	0.61
Minimum	−0.8	−0.2	−0.8
Median	0.6	0.2	0.2
Maximum	1.7	0.8	1.7
Missing, *n* (%)	3 (11.1)	10 (52.6)	12 (32.4)

Total confidence score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Change from baseline (T0) at 12 months (T3)[c]			
n (%)	11 (61.1)	10 (52.6)	21 (56.8)
Mean	0.7	0.3	0.5
SD	0.49	0.43	0.50
Minimum	0.0	−0.2	−0.2
Median	0.7	0.3	1.0
Maximum	1.7	1.0	1.7
Missing, *n* (%)	7 (38.9)	9 (47.4)	16 (43.2)

a Total confidence score ranges between 1 and 5; higher scores correspond to higher levels of confidence.
b Participants had no data recorded for the outcome.
c Calculated only for SO participants with a baseline and 12-month measurement reported.

Knowledge of what to do when faced with a seizure

Total knowledge score (patient participants)

Total knowledge score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	26 (100.0)	25 (100.0)	51 (100)
Mean	9.0	9.0	9.0
SD	4.05	4.19	4.08
Minimum	0	0	0
Median	10	11	11
Maximum	13	13	13
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
12 months (T3)			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	9.4	9.4	9.4
SD	3.68	3.69	3.63
Minimum	1	3	1
Median	10.5	11.0	6.0
Maximum	13	13	13
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	18 (69.2)	17 (68.0)	35 (68.6)
Mean	−0.4	0.8	0.1
SD	3.62	3.15	3.41
Minimum	−8	−8	−8

Total knowledge score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Median	0	1	0
Maximum	7	5	7
Missing, *n* (%)	8 (30.8)	8 (32.0)	16 (31.4)

a Knowledge score is calculated based on the number of questions about epilepsy answered correctly out of a total of 13.
b Calculated only for patient participants with a baseline and 12-month measurement reported.

Total knowledge score (significant other participants)

Total knowledge score[a]	Treatment arm: SAFE plus TAU	Treatment arm: TAU	Total
Baseline (T0)			
n (%)	18 (100.0)	19 (100.0)	37 (100.0)
Mean	9.9	7.7	8.8
SD	3.07	4.19	3.81
Minimum	4	1	1
Median	11	7	9
Maximum	13	13	13
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
12 months (T3)			
n (%)	15 (83.3)	13 (68.4)	28 (75.7)
Mean	7.4	8.15	7.8
SD	5.36	5.40	5.29
Minimum	0	0	0
Median	9	11	9.5
Maximum	13	13	13
Missing, *n* (%)	3 (16.7)	6 (31.6)	9 (24.3)
Change from baseline (T0) at 12 months (T3)[b]			
n (%)	15 (83.3)	13 (68.4)	28 (75.7)
Mean	−2.0	−0.8	−1.5
SD	5.03	5.01	4.96
Minimum	−12	−12	−12
Median	0	0	0
Maximum	4	8	8
Missing, *n* (%)	3 (16.7)	6 (31.6)	9 (24.3)

a Knowledge score is calculated based on the number of questions about epilepsy answered correctly out of a total of 13.
b Calculated only for SO participants with a baseline and 12-month measurement reported.

Appendix 19 Adverse events occurring during pilot trial in descending order, according to frequency overall

Adverse event		Treatment arm				Total	
		SAFE plus TAU		TAU			
Category of event (e.g. body system)	Event	Events, *n*	Patients, *n* (%)	Events, *n*	Patients, *n* (%)	Events, *n*	Patients, *n* (%)
Eyes, ear, nose and throat	Problem with eyes and sinuses	0	0 (0.0)	1	1 (9.1)	1	1 (5.6)
Genitourinary	Overnight hospital admission required owing to urinary tract infection (pre-existing)	0	0 (0.0)	1	1 (9.1)	1	1 (5.6)
Haematological	Dislocated shoulder	0	0 (0.0)	1	1 (9.1)	1	1 (5.6)
Neoplasia[a]	Change in seizure pattern	1	1 (14.3)	0	0 (0.0)	1	1 (5.6)
	Increase in seizure frequency	1	1 (14.3)	0	0 (0.0)	1	1 (5.6)
Neurological	Increased seizures; medications changed	1	1 (14.3)	3	3 (27.3)	4	4 (22.2)
	Increased seizures (shift patterns at work)	1	1 (14.3)	0	0 (0.0)	1	1 (5.6)
	New seizure type; frequent absence seizures as well as usual seizure types	1	1 (14.3)	0	0 (0.0)	1	1 (5.6)
	Seizure frequency; sodium levels requiring in patient monitoring	0	0 (0.0)	1	1 (9.1)	1	1 (5.6)
	Seizures more severe (tonic–clonic)	0	0 (0.0)	1	1 (9.1)	1	1 (5.6)
	Vagus nerve stimulation not working properly; going to hospital for observation	0	0 (0.0)	1	1 (9.1)	1	1 (5.6)
Respiratory	Increases number of seizures owing to chest infection and antibiotics	0	0 (0.0)	1	1 (9.1)	1	1 (5.6)
Other	Adverse events occurring during pilot trial increase in the number of fits owing to being pregnant/just given birth	0	0 (0.0)	2	1 (9.1)	2	1 (5.6)
	Diagnosis of status epilepticus	1	1 (14.3)	0	0 (0.0)	1	1 (5.6)
	Vertigo	0	0 (0.0)	1	1 (9.1)	1	1 (5.6)
Total		6	6 (100.0)	13	11 (100.0)	19	18 (100.0)

a Two participants were under investigation to determine whether or not a brain tumour could be the cause of their seizure changes; hence, the event was classified as neoplasia rather than neurological.

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