Clinical effectiveness of the psychological therapy Mental Health Intervention for Children with Epilepsy in addition to usual care compared with assessment-enhanced usual care alone: a multicentre, randomised controlled clinical trial in the UK

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See Comment page 1208

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Summary

Background Mental health difficulties are common in children and young people with chronic health conditions, but many of those in need do not access evidence-based psychological treatments. The study aim was to evaluate the clinical effectiveness of integrated mental health treatment for children and young people with epilepsy, a common chronic health condition known to be associated with a particularly high rate of co-occurring mental health difficulties.

Methods We conducted a parallel group, multicentre, open-label, randomised controlled trial of participants aged 3–18 years, attending epilepsy clinics across England and Northern Ireland who met diagnostic criteria for a common mental health disorder. Participants were randomised (1:1; using an independent web-based system) to receive the Mental Health Intervention for Children with Epilepsy (MICE) in addition to usual care, or assessment-enhanced usual care alone (control). Children and young people in both groups received a full diagnostic mental health assessment. MICE was a modular psychological intervention designed to treat common mental health conditions in children and young people using evidence-based approaches such as cognitive behaviour therapy and behavioural parenting strategies. Usual care for mental health disorders varied by site but typically included referral to appropriate services. Participants, along with their caregivers, and clinicians were not masked to treatment allocation but statisticians were masked until the point of analysis. The primary outcome, analysed by modified intention-to-treat, was the parent-report Strengths and Difficulties Questionnaire (SDQ) at 6 months post-randomisation. The study is complete and registered with ISRCTN (57823197).

Findings 1401 young people were potentially deemed eligible for study inclusion. Following the exclusion of 531 young people, 870 participants were assessed for eligibility and completed the SDQ, and 480 caregivers provided consent for study inclusion between May 20, 2019, and Jan 31, 2022. Between Aug 28, 2019, and Feb 21, 2022, 334 participants (mean ages 10·5 years [SD 3·6] in the MICE group *vs* 10·3 [4·0] in control group at baseline) were randomly assigned to an intervention using minimisation balanced by age, primary mental health disorder, diagnosis of intellectual disability, and autistic spectrum disorder at baseline. 168 (50%) of the participants were female and 166 (50%) were male. 166 participants were randomly assigned to the MICE group and 168 were randomly assigned to the control group. At 6 months, the mean SDQ difficulties for the 148 participants in the MICE group was 17·6 (SD 6·3) and 19·6 (6·1) for the 148 participants in the control group. The adjusted effect of MICE was –1·7 (95% CI –2·8 to –0·5; p=0·0040; Cohen's d, 0·3). 14 (8%) patients in the MICE group experienced at least one serious adverse event compared with 24 (14%) in the control group. 68% percent of serious adverse events (50 events) were admission due to seizures.

Interpretation MICE was superior to assessment-enhanced usual care in improving symptoms of emotional and behavioural difficulties in young people with epilepsy and common mental health disorders. The trial therefore shows that mental health comorbidities can be effectively and safely treated by a variety of clinicians, utilising an integrated intervention across ages and in the context of intellectual disability and autism. The evidence from this trial suggests that such a model should be fully embedded in epilepsy services and serves as a model for other chronic health conditions in young people.

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Introduction

People with chronic health conditions are two to four times more likely to experience mental health difficulties than are their physically healthy counterparts.[1] This is particularly seen in children and young people with epilepsy—up to 60% of those with epilepsy have associated mental health difficulties[2] and many have more than one mental health difficulty.[3] A high proportion of people with epilepsy can show symptoms consistent with mental health difficulties before the first recognised seizure, suggesting that a contributory factor to this relationship is shared neurobiology.[3] Mental health disorders in young people with chronic health conditions are associated with reduced quality of life,[4] poorer physical health,[5] worse mental health in caregivers,[6] and increased chance of death.[7] This well-known association between mental and physical health, particularly highlighted in people with epilepsy, has resulted in integrated mental and physical health care becoming a global priority, with recent position statements from WHO and International League Against Epilepsy.[8–10] Yet often, mental health difficulties in youth with chronic health conditions remain undiagnosed, their treatment remains inadequate, and services are unable to integrate physical and mental health care.[11,12]

Barriers to managing mental health difficulties in epilepsy include a lack of trained mental health specialists and standardised assessment procedures.[13] Training professionals from within physical health-care services to deliver evidence-based assessment and treatments for people with mental health difficulties has been successfully used for adults with other chronic health conditions.[14]

A key factor that might be associated with maintaining engagement in psychological interventions over time is the ability of the intervention to adapt flexibly to the physical and mental health needs of the person for whom it is intended.[15] One example of a highly flexible, evidence-based psychological intervention that can address multiple simultaneous mental health comorbidities is the Modular Approach to Therapy for Children with Anxiety, Depression, Trauma or Conduct problems (MATCH-ADTC).[16–19]

Using epilepsy as an example, this trial aimed to compare the clinical effectiveness of a personalised modular psychological intervention (Mental Health Intervention for Children with Epilepsy [MICE]) plus

Research in context

Evidence before this study

Many research trials and meta-analyses have shown the efficacy of psychological treatments for anxiety, depression, and conduct disorders in children and young people. Such treatments are also effective when delivered in a modular format designed to enable multiple disorders to be addressed within the same intervention. Separately, many studies have indicated that children and young people with neurological disorders such as epilepsy are more likely than their healthy peers to experience common mental health difficulties and often experience multiple difficulties (eg, anxiety and behavioural challenges). Before conducting this study, we conducted a randomised pilot trial using telephone-guided self-help for mental health difficulties in neurological conditions and a systematic review and linked evidence synthesis on psychological interventions in young people with mental health difficulties in the context of chronic health conditions.
We searched PubMed from database inception on Feb 5, 2024, with the terms ((“randomised”) OR (“randomized”) OR (“trial”)) AND ((“epilepsy”) OR (“neurological”) AND ((“children”) OR ((“youth”) OR (“young people”)) AND ((“modular”) AND (“therapy”)) with no language restrictions. We retrieved no studies investigating a modular psychological intervention for children and young people with epilepsy.

Added value of this study

To our knowledge, this is the first full-scale trial of a modular psychological intervention designed specifically to treat multiple co-occurring common mental health difficulties in the context of a chronic health condition in children and young people. The results demonstrate that it is possible to successfully treat mental health difficulties in the context of a chronic health condition and to integrate mental and physical healthcare. They also show that it is possible to achieve these outcomes with therapists who do not have substantial training in mental health interventions, including epilepsy specialist nurses and graduate psychologists. Furthermore, the results show that a wide range of children and young people benefit from this approach, including those aged 3–18 years, those with intellectual disabilities, and those who are neurodivergent.

Implications of all the available evidence

The evidence suggests that children and young people who have chronic health conditions, such as epilepsy, should have their mental health needs identified, and should be offered evidence-based interventions. Such interventions should be offered from within the physical health-care service. Future research should investigate the use of this model within other chronic health conditions. These findings have implications for services, commissioners, researchers, clinicians, and affected families in understanding the treatment of multiple mental health difficulties in the context of chronic health conditions, and in informing health-care systems on service planning.

usual care with assessment-enhanced usual care alone (control group). MICE was delivered remotely (ie, via telephone or videoconferencing software) by clinicians within physical health-care services. In this study, we report on the clinical effectiveness outcomes. The full health economic analyses will be published elsewhere to provide in-depth data on cost-effectiveness. Qualitative data were also collected and will be reported separately. It was hypothesised that MICE plus usual care would be superior to assessment-enhanced usual care in improving emotional and behavioural symptoms.

Methods

Study design and participants

The MICE trial was a multi-centre, parallel group, superiority, randomised controlled trial to evaluate the efficacy of MICE therapy, delivered remotely for youth with epilepsy and common mental health difficulties (anxiety, depression, disruptive behaviour, or a combination of these) delivered from within epilepsy services by clinicians who did not have substantial previous formal experience of psychological therapy.

The trial was conducted across 13 epilepsy services in England and Northern Ireland (six main sites and seven referring sites [that could refer participants into a main study site to participate in the trial but did not consent participants themselves]; appendix p 10).

See Online for appendix

Participant inclusion criteria were: attendance at UK National Health Service epilepsy clinics; age 3–18 years; scored above the pre-specified threshold on the Strengths and Difficulties Questionnaire (SDQ)[20] for mental health symptoms (combination of raised Total Difficulty score [≥14] and raised Impact score [≥2]); and met DSM-5 diagnostic criteria for a mental health disorder on the Development and Wellbeing Assessment (DAWBA),[21] with a caregiver who was willing to take part in the study. Participants who had an intellectual disability or existing diagnosis of autism spectrum disorder were included in the trial, as long as the intellectual disability did not prevent them from participating appropriately. The published protocol[20] and appendix (p 3) provide full details of all measures and inclusion and exclusion criteria. The trial was approved by the South Central-Oxford Research Ethics Committee (18/SC/0250). Full written informed consent was provided by parents or caregivers, and consent or assent by children and young people for cases in which this was appropriate.

Randomisation and masking

A research assistant who was independent of the treatment and outcome data collection randomly assigned participants to the MICE intervention group or the assessment-enhanced usual care control group using an independent web-based online system in a 1:1 ratio. Randomisation used a minimisation algorithm incorporating a random element; minimisation factors comprised primary mental health disorder (anxiety, depression, disruptive behaviour, or trauma), caregiver-reported presence of existing formal autism spectrum disorder diagnosis (yes or no), age (younger than 11 years or 11 years and older), and caregiver-reported presence of intellectual disability (yes or no). Allocation was concealed before assignment to prevent allocation bias. Trial participants, their caregiver, and clinicians were not masked to treatment allocation. Trial statisticians were masked until the point of analysis. Participant outcome assessments were done by researchers who were masked at both timepoints to treatment allocation. Participants were reminded about the importance of masking at each follow-up timepoint.

For more on the **web-based randomisation system** see https://www.sealedenvelope.com

Procedures

Participants were recruited from screening within epilepsy clinics at one of the main participating sites, via referral from one of the clinicians in the main participating sites, or referral from a participant identification centre. Specifically, families could be approached in the clinic or hospital by a member of the research team and asked a few brief questions to determine their eligibility for participation. Depending on their answers to these questions, they were asked to complete the SDQ. Families could also be identified by clinicians who were familiar with them. In these situations, the clinical team could make contact with the family to ask them if they were interested in being contacted by the MICE trial team or wished to contact the MICE team directly. They were then asked the same questions to establish eligibility. The caregiver (and child, if appropriate) had to provide verbal consent to complete the SDQ and agree to being contacted with the results. They were offered the choice of completing the SDQ in clinic, online, or alone in their own time or with support (via the telephone, online, or in person).

If the results of the SDQ indicated that the participant could meet inclusion criteria, the caregiver was given the Participant Information Sheet and Informed Consent Form. The young participant was also provided with an age-appropriate Participation Information Sheet and consent or assent form, where appropriate. Following written or oral consent and assent, caregivers were invited to complete a full computerised psychiatric diagnostic assessment of their child's mental health, the DAWBA,[21] which was rated for presence or absence of mental health disorders by a trained clinician. Those meeting diagnostic criteria for anxiety, depression, or a disruptive behaviour disorder were invited to complete the remainder of the baseline measures before being randomised. Participant characteristics, including demographics, age of epilepsy diagnosis, and seizure types were recorded through caregiver self-report and review of medical records. All demographic characteristics were recorded by caregivers, including gender (male, female, other, or prefer not to say). Follow-up measures were completed at 6 months post-randomisation.

Usual care for mental health disorders varied by site but typically included referral to child and adolescent mental health services or hospital-based paediatric psychology services (figure 1). The arm was considered as assessment-enhanced usual care since the detailed diagnostic results of the DAWBA were provided as information to the caregiver, General Practitioner, and other clinical team members involved. This report might have enabled families or clinicians to better understand their child's difficulties and could be used to refer children to mental health services as required.

The MICE therapy intervention was derived from MATCH-ADTC, a personalised modular cognitive-behavioural intervention delivered over the telephone or via video conferencing, with epilepsy-relevant content integrated throughout and an additional compulsory epilepsy-specific module and three optional epilepsy-related modules. The epilepsy materials were developed and finalised in earlier stages of the programme of research.[16,22,23] MICE therapy involved an initial assessment following weekly phone or online video calls with the clinician. Face-to-face therapy sessions were permitted if clinically indicated or strongly preferred by the family. The intervention could be delivered to the caregiver or child depending on the child's developmental level and presenting difficulty. In general, intervention sessions were delivered to caregivers with or without the child present for those children with one or more of the following: primary problem area related to behavioural challenges, younger children (younger than 11 years), or children with intellectual disabilities. In other cases (ie, anxiety, depression, no intellectual disability, older children, and young people), the intervention was delivered to the young person with or without a caregiver present. The final decision regarding who attended each session would be made by the family in collaboration with the therapist.

Session by session measurement of symptoms and progress towards self-identified goals was part of the intervention. These session-by-session measures were used for clinical purposes rather than as research outcomes and are not reported in the present study. The therapy was comprised of up to 20 sessions plus two booster sessions. All therapy sessions were delivered within 6 months of randomisation although booster sessions could occur between 6-months and 12-months post-randomisation. Young people in the MICE group also accessed usual care for the mental health difficulties if required.

Therapist Competence and Fidelity to the protocol was established by review of an expert therapist accredited by the British Association for Behavioural and Cognitive Psychotherapies. Adherence scores were based on a review of all treatment sessions in accordance with the integrity principles of MATCH-ADTC. The content of all treatment sessions recorded by therapists were categorised as either all planned content, some planned content, or no planned content, and the percentage of

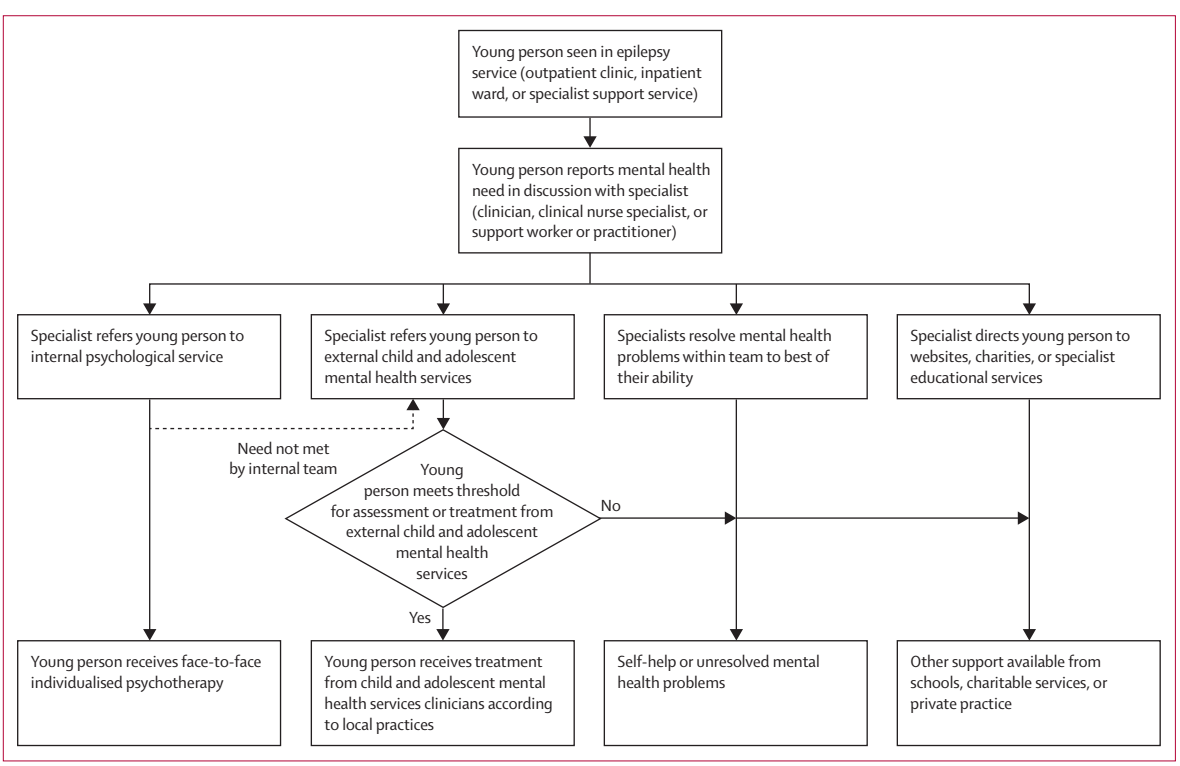

Figure 1: **Usual care for mental health disorders in children and young people with epilepsy**

sessions that adhered to the content and sequencing of the treatment protocol was calculated for each patient. Audiotapes of 10% of the sessions were selected at random to ensure session content matched that reported by therapists and were also rated for therapist competence using the Cognitive Therapy Rating Scale Revised (CTS-R). Additionally, 10% of these were selected at random and double-rated by an external British Cognitive Behaviour Therapy accredited expert.

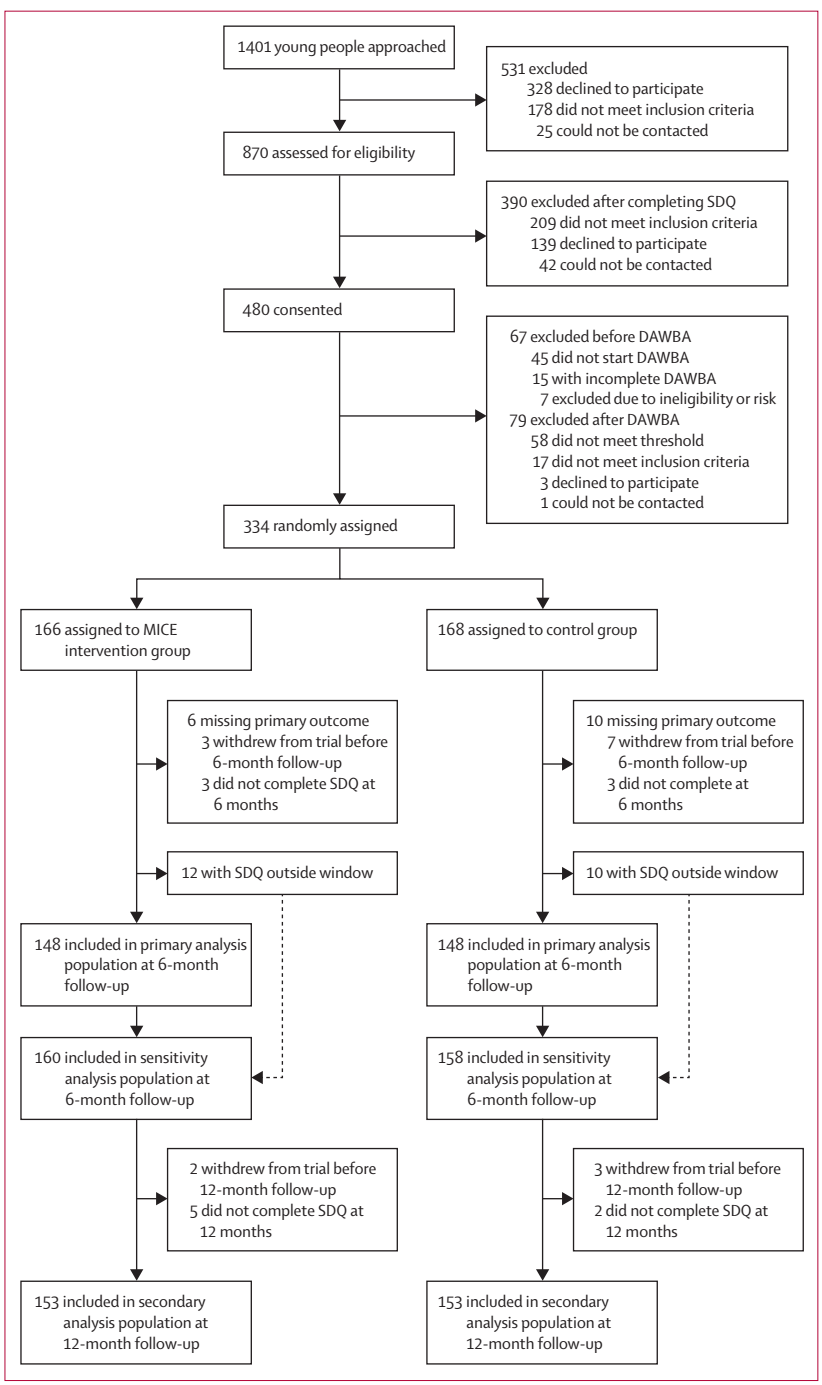

Figure 2: **Trial profile**
SDQ=Strengths and Difficulties Questionnaire. DAWBA=Development and Wellbeing Assessment.

Outcomes

The primary effectiveness clinical endpoint was at 6-months post-randomisation with a subsequent secondary clinical endpoint with associated health economic analyses at 12 months post-randomisation. All outcomes were caregiver reported for data completeness, as self-report versions were burdensome and not suitable for the ability range of all participants in the trial. The primary outcome of SDQ has been validated across the age range of participants in the trial. The secondary measures were not all validated for use across the full age range of the participants.

The primary outcome measure was the SDQ Total Difficulties Score reported by the parent or carer at 6 months post-randomisation, which has a range of 0–40, in which a higher score indicates more mental health difficulties. Scores of 0–13 are close to average, 14–16 are slightly raised, 17–19 are high, and 20–40 are very high. The primary outcome was assessed in the modified intention-to-treat population, with participants with available data at 6 months analysed according to their randomised group.

A range of secondary outcomes were measured which were either child-related or caregiver-related. The first child-related secondary outcome was SDQ total difficulties, which was assessed at 12 months in addition to the following secondary outcomes measured at 6 months and 12 months post-randomisation. The next secondary outcome was the SDQ Impact Scale. This has a range of 0–10 and assesses resultant impairment across a range of domains (home, school, and leisure). Scores of 0 are close to average, 1 is slightly raised, 2 is high, and 3–10 is very high. The next secondary outcome was the Revised Child Anxiety and Depression Scale (RCADS). This is a 47-item measure of anxiety disorders and depression, with six subscales and a total raw range of 0 to 141. Clinical ranges are considered in terms of age and gender for individual children after converting raw scores to T scores. A further outcome was the service use measured using the Child and Adolescent Service Use Schedule (CA-SUS), which was developed and then applied in a range of populations of young people with mental health problems. Other secondary outcomes were the Hague Seizure Severity Scale, which rates carers' subjective experiences of the severity of their child's seizures, with range 13 to 54, and the Paediatric Quality of Life Epilepsy Module (PedsQL), which measures the effect of epilepsy on a young person's quality of life with four subscales and a total score ranging from 0 to 100.

The number of serious adverse events was reported using the National Institutes of Health Common Terminology Criteria for Adverse Events (version 5). A serious adverse event was defined as an event that was life threatening; required or prolonged existing hospital

admission; resulted in death or a persistent or severe disability or incapacity; or resulted in an important medical condition, regardless of relatedness to the trial intervention. The numbers of serious adverse events were reported for all participants who were randomly assigned to a group in the study.

Two caregiver-related outcomes were assessed. The Patient Health Questionnaire (PHQ-9), which is a nine-item measure of depression in adults completed by the caregiver about their own mental health, with range 0 to 27, and the Generalised Anxiety Disorder Assessment (GAD-7), which is a seven-item measure of generalised anxiety disorder, completed by the caregiver about their own mental health, with range 0 to 21. Additional measures (the CHU-9D and EQ-5D-5L) were also completed as part of the health economic analysis and the results of these are not reported in the present study. The secondary outcomes were assessed in the modified intention-to-treat population, with participants with available data analysed according to their randomised group.

Statistical analysis

The trial aimed to recruit a total sample of 334 young people to detect an effect size of 0·3, with 80% power and at the 5% (two-sided) level of significance. The sample size calculation assumed an SD of 1, an average of 14 children per therapist, an Intracluster Coreelation Coeffecient of 0·01 for therapist effects, a correlation of 0·5 between baseline and follow-up SDQ, and a loss to follow-up rate of 10%.[24] All primary analyses were conducted according to the modified intention-to-treat principle, in which all patients who were randomly assigned to an intervention were analysed in their allocated group whether or not they received their randomised treatment. For the primary analysis, data were not imputed for the participants who did not have outcome data for the relevant measure in line with the pre-registered statistical analysis plan. The primary analysis population included all patients with SDQ data reported within the time window defined in the protocol (–1 week to +3 weeks around the 6-month post-randomisation follow-up timepoint).

We assessed the impact of missing data by performing a sensitivity analysis on the primary outcome including all out-of-window responders. Additional adjustment of baseline seizure severity was also performed for the primary outcome. A secondary post-hoc analysis in which the missing primary outcome data were imputed was also conducted.

A partially clustered, mixed-effects linear regression model was used to determine whether there was any between-group difference in SDQ total difficulties score at 6 months. The model included fixed effects for intervention group, baseline SDQ total difficulties score, and the minimisation factors. In this trial, patients in the MICE group who were seen by the same clinician were grouped according to their clinician and this has been accounted for in the model using a random clinician factor. The model was fitted using restricted maximum likelihood estimation. The standardised effect size was determined using Cohen's d.

	MICE group (n=166)	Control group (n=168)	Total (n=334)
Age, years	10·5 (3·6)	10·3 (4·0)	10·4 (3·8)
Age, years			
Younger than 11	99 (60%)	101 (60%)	200 (60%)
11 or older	67 (40%)	67 (40%)	134 (40%)
Gender			
Female	81 (49%)	87 (52%)	168 (50%)
Male	85 (51%)	81 (48%)	166 (50%)
Ethnicity			
White or White British	122 (73%)	116 (69%)	238 (71%)
Mixed	18 (11%)	18 (11%)	36 (11%)
Asian or Asian British	11 (7%)	12 (7%)	23 (7%)
Black or Black British	7 (4%)	16 (10%)	23 (7%)
Other ethnic groups	4 (2%)	5 (3%)	9 (3%)
Did not disclose	4 (2%)	1 (1%)	5 (1%)
Socio economic status*			
Most deprived 20%	17/155 (11%)	23/160 (14%)	40/315 (13%)
20–40%	42/155 (27%)	40/160 (25%)	82/315 (26%)
40–60%	38/155 (25%)	40/160 (25%)	78/315 (25%)
60–80%	20/155 (13%)	24/160 (15%)	44/315 (14%)
Least deprived 20%	38/155 (25%)	33/160 (21%)	71/315 (23%)
Primary mental health disorder			
Anxiety	66 (40%)	67 (40%)	133 (40%)
Depression	7 (4%)	9 (5%)	16 (5%)
Disruptive behaviour	93 (56%)	92 (55%)	185 (55%)
Existing diagnosis of autistic spectrum disorder			
No	126 (76%)	128 (76%)	254 (76%)
Yes	40 (24%)	40 (24%)	80 (24%)
Intellectual disability			
No	99 (60%)	101 (60%)	200 (60%)
Yes	67 (40%)	67 (40%)	134 (40%)
Time since epilepsy diagnosis, years	5·5 (3·7)	5·3 (3·7)	5·4 (3·7)
Number of mental health disorders			
One	105 (63%)	110 (65%)	215 (64%)
More than one	61 (37%)	58 (35%)	119 (36%)
Has had seizures in the past 3 months			
No	62 (37%)	54 (32%)	116 (35%)
Yes	104 (63%)	114 (68%)	218 (65%)
Hague Seizure Severity Scale†	34·4 (7·9)	33·3 (8·0)	33·8 (8·0)
SDQ Total Difficulties	23·0 (5·2)	23·5 (5·4)	23·2 (5·3)
SDQ Impact	7·0 (2·3)	7·1 (2·1)	7·1 (2·2)
PedsQL Epilepsy Module			
Impact	55·0 (18·9)	53·8 (21·5)	54·4 (20·2)
Cognitive functioning	31·1 (28·1)	32·2 (26·1)	31·7 (27·1)
Sleep or rest	35·8 (26·6)	31·7 (27·7)	33·7 (27·2)
Executive functioning	30·6 (24·6)	32·8 (27·4)	31·7 (26·1)
Mood/behaviour	39·4 (16·0)	38·5 (18·6)	38·9 (17·3)

(Table 1 continues on next page)

	MICE group (n=166)	Control group (n=168)	Total (n=334)
(Continued from previous page)			
RCADS score			
Total anxiety and depression	66·6 (17·4)	66·6 (16·6)	66·6 (17·0)
Depression	70·9 (15·7)	70·9 (16·9)	70·9 (16·3)
Total anxiety	63·2 (17·7)	63·1 (16·6)	63·1 (17·2)
Generalised anxiety	58·6 (16·8)	58·5 (16·1)	58·6 (16·4)
Obsessions/compulsions	53·3 (12·3)	54·2 (13·0)	53·8 (12·7)
Panic	63·9 (21·1)	64·1 (22·3)	64·0 (21·7)
Separation anxiety	68·2 (19·9)	70·0 (20·9)	69·1 (20·4)
Social phobia	57·6 (18·6)	56·1 (17·0)	56·9 (17·8)
Parents and caregiver characteristics			
PHQ-9 score	5 (2–10)	6 (2–11)	5 (2–11)
GAD-7 score	6 (2–12)	6 (2–12)	6 (2–12)

Data are n (%), n/N (%), mean (SD), or median (IQR). MICE=Mental Health Intervention for Children with Epilepsy. SDQ=Strengths and Difficulties Questionnaire. PedsQL=Paediatric Quality of Life Epilepsy Module. RCADS=Revised Child Anxiety and Depression Scale. PHQ-9=Patient Health Questionnaire. GAD-7=Generalised Anxiety Disorder Assessment. *Data not available for all randomised patients. Percentages are based on 155 participants in the MICE group and 160 participants in the control group. †Score based on 104 participants in the MICE group and 114 participants in the control group who confirmed having a seizure in the past 3 months at baseline.

Table 1: **Baseline characteristics**

Secondary outcomes were evaluated using similar mixed models. Results are presented as adjusted treatment effect and the associated 95% CI. These confidence intervals for the secondary outcomes are not adjusted for multiple comparisons. Pre-specified subgroup analyses were performed for the primary outcome, to investigate presence of interaction between the effect of treatment and the minimisation factors. The preregistered statistical analysis plan included such subgroup analysis with age dichotomised as younger than 11 years and 11 years and older. This analysis was changed to include age as a continuous variate, which was considered more clinically meaningful. The trial is powered only on the primary outcome. All other analyses, including secondary and moderation analyses, have been considered to assess internal consistency. The proportion of patients experiencing at least one serious adverse event and the number of serious adverse events are described by group. We used STATA/MP 17.0 for all analyses.

Six substantial amendments were made and six deviations from the protocol were recorded (appendix pp 4–9). The trial was conducted and reported according to the published protocol[24] which was approved by an independent programme steering committee and a data monitoring and ethics committee. The data monitoring and ethics committee reviewed trial data and conduct at regular intervals throughout the trial. The trial was prospectively registered with the ISRCTN (ISRCTN57823197).

Role of the funding source

The funders had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Results

1401 young people (and their caregivers) were approached to be included in the study. 531 were excluded for declining to participate, not meeting inclusion criteria, or could not be contacted. 870 participants were assessed for eligibility and completed the SDQ and 480 caregivers provided consent for their child between May 20, 2019, and Jan 31, 2022. Of those who consented, 334 (70%) met all eligibility criteria and were randomly assigned to an intervention, 166 to the MICE group and 168 to the control group, between Aug 28, 2019, and Feb 21, 2022 (figure 2). Of those randomised, 16 patients (5%) withdrew from the trial before 6 months or had missing SDQ at the primary timepoint. A further 22 patients (7%) completed the SDQ outside the protocol-defined window and were not included in the primary outcome analysis; however, a sensitivity analysis was done to assess the effect of including these patients. The primary analysis population therefore included 296 patients (148 in each group) with reported outcome data (89% of those randomised) within the time window defined in the protocol and statistical analysis plan. 39 instances of unmasking of outcome assessors to treatment allocation were noted. The participants who did not complete the SDQ at 6 months were not systematically different from those who completed the SDQ at 6 months, with regard to age, gender, and ethnicity. The last participant completed the 6-month follow-up on Sept 28, 2022. Patient and caregiver characteristics at baseline are presented in table 1. The mean age of the participants was similar in both groups: 10·5 years (SD 3·6) in the MICE group versus 10·3 years (4·0) in the control group. 168 (50%) of the participants were female and 166 (50%) were male. Participants were balanced between treatment groups regarding the minimisation factors, age group, primary mental health disorder, and diagnosis of autism spectrum disorder and intellectual disability. A total of 80 (24%) participants had an existing diagnosis of autism spectrum disorder and 134 (40%) had intellectual disability at randomisation.

Of the 166 participants randomly assigned to the MICE group, 164 had at least one therapy session. The median number of sessions was 16 (IQR 12–19). There were 21 clinicians and therapist and clinician characteristics have been previously reported.[16]

Usual care was consistent with services' descriptions before the trial. Data from the CA-SUS demonstrated that both MICE and control groups accessed similar types of mental health services (table 2). However, 35% (48 of 136) of participants in the MICE group used any mental health service during the 6-month trial follow-up period, compared with 40% (57 of 144) in the control group, although the number of contacts in both groups was low. By the 12-month trial follow-up period, this increased to 51% (65 of 128) of participants in the MICE group compared to 60% (80 of 134) in the control group. The primary analysis population included 148 patients in the

	MICE group			Control group		
	Mean (SD)	Range	Proportion of participants who used the service	Mean (SD)	Range	Proportion of participants who used the service
Hospital mental health services						
T0 Inpatient mental health	0·00 (0·00)	0	0%	0·00 (0·00)	0	0%
T0–T1 Inpatient mental health	0·01 (0·09)	0–1	1%	0·00 (0·00)	0	0%
T0–T2 Inpatient mental health	0·01 (0·09)	0–1	1%	0·00 (0·00)	0	0%
T0 Outpatient mental health	0·11 (0·59)	0–5	4%	0·06 (0·26)	0–2	5%
T0–T1 Outpatient mental health	0·12 (0·46)	0–3	8%	0·13 (0·74)	0–6	4%
T0–T2 Outpatient mental health	0·21 (0·66)	0–3	12%	0·48 (2·02)	0–18	14%
Community mental health services						
T0 Education psychologist	0·11 (0·45)	0–4	8%	0·24 (0·74)	0–7	17%
T0–T1 Education psychologist	1·25 (4·67)	0–35	19%	0·88 (2·71)	0–15	19%
T0–T2 Education psychologist	1·88 (6·31)	0–43	28%	1·88 (4·80)	0–27	30%
T0 Child and Adolescent Mental Health Services	0·29 (1·30)	0–12	10%	0·15 (0·67)	0–6	8%
T0–T1 Child and Adolescent Mental Health Services	0·53 (2·07)	0–12	13%	0·40 (2·16)	0–24	11%
T0–T2 Child and Adolescent Mental Health Services	0·77 (2·34)	0–13	20%	0·86 (4·12)	0–44	18%
T0 Counsellor	0·27 (1·49)	0–10	7%	0·28 (1·30)	0–12	7%
T0–T1 Counsellor	0·24 (1·85)	0–18	4%	0·27 (2·12)	0–24	3%
T0–T2 Counsellor	0·30 (1·98)	0–18	3%	1·12 (4·29)	0–30	12%
Collected at follow-up only						
T0–T1 Clinical psychologist	0·20 (1·14)	0–12	7%	0·20 (0·87)	0–6	8%
T0–T2 Clinical psychologist	0·40 (2·31)	0–22	10%	0·56 (1·87)	0–12	17%
T0–T1 Community psychiatrist	0·05 (0·43)	0–4	1%	0·27 (1·61)	0–14	6%
T0–T2 Community psychiatrist	0·08 (0·63)	0–6	2%	0·41 (1·78)	0–14	11%
T0–T1 Family therapy	0·00 (0·00)	0	0%	0·01 (0·17)	0–2	1%
T0–T2 Family therapy	0·00 (0·00)	0	0%	0·39 (4·17)	0–48	2%

T0, baseline (use of services over the 3 months before baseline assessment); T1, 6-month follow-up; T2, 12-month follow-up. The mean is the average number of contacts per patient for whom data are available at that timepoint. The proportion of participants who used the service is the percentage of those for whom data are available at that timepoint who have reported using the service over the relevant time period.

Table 2: **Mental health service use at baseline and follow-up**

MICE intervention group and 148 patients in the control group. The mean SDQ total difficulties scores at 6 months were 17·6 (SD 6·3) in the MICE group, a change of –5·3 (SD 4·9) from baseline, compared with 19·6 (6·1) in the control group, a change of –3·8 (5·1) from baseline (figure 3; table 3). There was a significant between-group effect in favour of the MICE group on the primary outcome; the adjusted difference in SDQ total difficulties between patients in the MICE group and patients in the control group was –1·7 (95% CI –2·8 to –0·5; p=0·0040) at 6 months. The effect size (Cohen's d) was 0·3 (95% CI 0·1 to 0·6). Sensitivity analyses with inclusion of out-of-window responders (22 patients) and additional adjustment showed similar results to the primary model. An additional post-hoc supportive intention-to-treat analysis of the primary outcome with a threshold-based imputation method was conducted and showed similar results (appendix p 13). The treatment effect observed at 6 months was maintained at 12 months with an adjusted difference in SDQ difficulties of –2·0 (95% CI –3·2 to –0·9; p<0·0001; effect size 0·4) between groups.

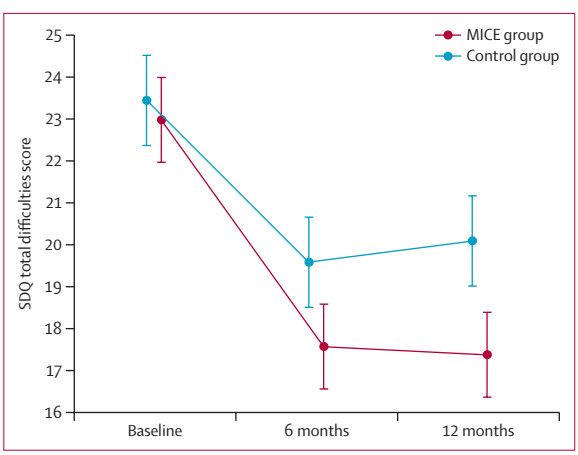

Figure 3: **Mean SDQ total difficulties score in the MICE and control groups**
Mean values presented in 95% CI at baseline, 6 months, and 12 months post-randomisation. MICE=Mental Health Intervention for Children with Epilepsy. SDQ=Strengths and Difficulties Questionnaire.

	MICE group				Control group				Adjusted difference	p value
	Number of participants	Baseline score	6-month follow-up score	Change in score between baseline and 6 months	Number of participants	Baseline score	6-month follow-up score	Change in score between baseline and 6 months		
SDQ difficulties: primary outcome	148	22·9 (5·0)	17·6 (6·3)	−5·3 (4·9)	148	23·3 (5·3)	19·6 (6·1)	−3·8 (5·1)	−1·7 (−2·8 to −0·5)	0·0040
SDQ difficulties: extended window	155	22·9 (5·1)	17·6 (6·4)	−5·4 (4·8)	152	23·4 (5·3)	19·5 (6·2)	−3·8 (5·0)	−1·6 (−2·7 to −0·5)	0·0040
SDQ difficulties: all data	160	22·9 (5·2)	17·5 (6·3)	−5·4 (4·9)	158	23·4 (5·3)	19·6 (6·2)	−3·8 (5·0)	−1·8 (−2·8 to −0·7)	0·0010
SDQ difficulties: adjusted for Hague Seizure Severity Scale	148	22·9 (5·0)	17·6 (6·3)	−5·3 (4·9)	148	23·3 (5·3)	19·6 (6·1)	−3·8 (5·1)	−1·7 (−2·8 to −0·5)	0·0040

Data are mean (SD) or mean (95% CI). MICE=Mental Health Intervention for Children with Epilepsy. SDQ=Strengths and Difficulties Questionnaire.

Table 3: **Effect of MICE adjusted for minimisation factors and baseline SDQ levels, including sensitivity models**

	MICE group				Control group				Adjusted difference	p value
	Number of participants	Baseline	6-month follow-up score	Change in score between baseline and 6 months	Number of participants	Baseline	6-month follow-up score	Change in score between baseline and 6 months		
SDQ impact	160	7·0 (2·3)	2·8 (2·6)	−4·2 (3·1)	158	7·1 (2·1)	4·1 (2·8)	−2·9 (2·9)	−1·2 (−1·9 to −0·6)	<0·0001
PedsQL Epilepsy Module										
Impact	130	55·0 (18·9)	58·7 (20·3)	3·1 (16·7)	123	53·8 (21·5)	53·9 (21·9)	0·7 (16·1)	3·3 (−0·5 to 7·1)	0·090
Cognitive functioning	130	31·1 (28·1)	30·5 (26·3)	−0·2 (19·1)	123	32·2 (26·1)	30·6 (24·0)	−2·1 (16·1)	1·7 (−2·2 to 5·7)	0·39
Sleep or rest	130	35·8 (26·6)	41·5 (26·7)	5·1 (24·1)	123	31·7 (27·7)	37·4 (25·3)	4·7 (24·1)	2·8 (−3·0 to 8·7)	0·34
Executive functioning	130	30·6 (24·6)	38·0 (25·0)	7·2 (19·0)	123	32·8 (27·4)	32·9 (24·7)	−1·5 (18·7)	7·1 (2·7 to 11·5)	0·0020
Mood or behaviour	130	39·4 (16·0)	49·2 (15·5)	10·2 (17·3)	123	38·5 (18·6)	41·7 (20·7)	3·2 (18·0)	7·1 (3·2 to 11·1)	<0·0001
Hague Seizure Severity Scale	72	34·4 (7·9)	37·0 (8·1)	1·1 (5·3)	82	33·3 (8·0)	35·1 (8·8)	2·7 (5·5)	−1·3 (−3·3 to 0·6)	0·17
RCADS										
Total anxiety and depression	132	66·6 (17·4)	59·9 (15·4)	−7·2 (15·0)	126	64·1 (18·1)	66·6 (16·6)	−2·8 (12·0)	−4·3 (−7·3 to −1·2)	0·020
Depression	132	70·9 (15·7)	64·3 (14·6)	−7·4 (15·0)	126	70·9 (16·9)	69·0 (18·8)	−2·6 (12·4)	−4·6 (−7·8 to −1·4)	0·0040
Total anxiety	132	63·2 (17·7)	57·4 (15·5)	−6·3 (14·4)	126	63·1 (16·6)	60·6 (17·9)	−2·6 (12·1)	−3·6 (−6·6 to −0·6)	0·020
Generalised anxiety	132	58·6 (16·8)	53·9 (12·8)	−5·3 (12·9)	126	58·5 (16·1)	55·6 (15·2)	−2·9 (12·0)	−2·1 (−4·7 to 0·5)	0·12
Obsessions or compulsions	132	53·3 (12·3)	52·4 (9·7)	−1·1 (11·8)	126	54·2 (13·0)	53·6 (13·5)	−0·4 (10·7)	−1·5 (−4·3 to 1·2)	0·27
Panic	132	63·9 (21·1)	59·3 (20·1)	−5·5 (21·4)	126	64·1 (22·3)	63·6 (27·5)	−0·4 (17·8)	−4·8 (−9·4 to −0·2)	0·040
Separation anxiety	132	68·2 (19·9)	61·5 (16·6)	−7·0 (14·8)	126	70·0 (20·9)	66·1 (19·9)	−3·3 (14·9)	−4·2 (−7·4 to −0·9)	0·010
Social phobia	132	57·6 (18·6)	53·4 (16·9)	−5·3 (13·5)	126	56·1 (17·0)	54·2 (17·3)	−2·5 (12·5)	−2·1 (−5·0 to 0·8)	0·16
PHQ-9	129	6·5 (5·8)	5·9 (4·8)	−0·6 (5·2)	123	7·1 (6·0)	7·4 (5·7)	0·9 (5·2)	−1·6 (−2·8 to −0·3)	0·020
GAD-7	129	7·3 (5·8)	6·2 (4·7)	−1·0 (5·3)	123	7·2 (5·5)	7·6 (5·1)	0·8 (5·2)	−1·5 (−2·8 to −0·3)	0·020

Data are mean (SD) or mean (95% CI), unless otherwise specified. MICE=Mental Health Intervention for Children with Epilepsy. SDQ=Strengths and Difficulties Questionnaire. PedsQL=Paediatric Quality of Life Epilepsy Module. RCADS=Revised Child Anxiety and Depression Scale. PHQ-9=Patient Health Questionnaire. GAD-7=Generalised Anxiety Disorder Assessment. *Data from 72 MICE and 82 control participants who reported having a seizure at baseline and at 6 months post-randomisation.

Table 4: **Adjusted difference in secondary outcome scores between MICE and control groups at baseline and 6 months post-randomisation**

All differences in secondary outcomes were in favour of the MICE group (tables 4 and 5). There was a significant difference in SDQ impact scores between the MICE and control groups at 6 months (difference, −1·2 [95% CI −1·9 to −0·6]) and at 12 months (difference, −1·4 [−2·0 to −0·8]). There was also a significant difference between the groups in caregivers' depression levels measured by the PHQ-9 (difference, −1·6 [95% CI −2·8 to −0·3]) and anxiety levels measured by the GAD-7 (difference, −1·5 [−2·8 to −0·3]) at 6 months.

	MICE group				Control group				Adjusted difference	p value
	Number of participants	Baseline	12-month follow-up score	Change in score between baseline and 12 months	Number of participants	Baseline	12-month follow-up score	Change in score between baseline and 12 months		
SDQ total difficulties	153	22·8 (5·1)	17·4 (6·4)	−5·4 (5·1)	153	23·7 (5·4)	20·1 (6·8)	−3·6 (5·3)	−2·0 (−3·2 to −0·9)	<0·0001
SDQ impact	153	7·0 (2·3)	3·0 (2·8)	−4·0 (3·1)	153	7·1 (2·1)	4·4 (3·0)	−2·7 (2·9)	−1·4 (−2·0 to −0·8)	<0·0001
PedsQL Epilepsy Module										
Impact	132	55·0 (18·9)	60·0 (21·0)	4·4 (19·9)	123	53·8 (21·5)	55·0 (24·8)	1·5 (19·3)	3·5 (−1·2 to 8·0)	0·13
Cognitive functioning	132	31·1 (28·1)	32·0 (28·4)	0·6 (21·0)	123	32·2 (26·1)	30·0 (26·2)	−2·5 (19·2)	3·0 (−2·7 to 8·7)	0·30
Sleep or rest	132	35·8 (26·6)	41·0 (28·3)	5·2 (28·1)	123	31·7 (27·7)	38·5 (27·3)	5·1 (26·2)	1·1 (−4·8 to 7·0)	0·72
Executive functioning	132	30·6 (24·6)	37·9 (26·2)	6·9 (19·2)	123	32·8 (27·4)	35·1 (27·5)	2·3 (18·4)	4·2 (−0·5 to 8·8)	0·080
Mood or behaviour	132	39·4 (16·0)	47·8 (19·5)	9·1 (20·1)	123	38·5 (18·6)	43·3 (20·6)	6·3 (20·2)	3·6 (−0·9 to 8·1)	0·12
Hague Seizure Severity Scale*	72	21·5 (17·8)	34·8 (8·6)	6·1 (15·6)	67	22·6 (16·9)	33·7 (8·0)	5·0 (11·3)	−1·3 (−3·1 to 0·5)	0·16
RCADS										
Total anxiety and depression	135	66·6 (17·4)	60·0 (17·4)	−6·9 (16·3)	124	66·4 (17·5)	66·6 (16·6)	−2·1 (14·0)	−5·5 (−9·4 to −1·7)	0·0040
Depression	135	70·9 (15·7)	64·7 (17·1)	−5·9 (15·5)	124	70·9 (16·9)	69·6 (19·1)	−3·7 (15·6)	−3·2 (−6·7 to 0·4)	0·080
Total anxiety	135	63·2 (17·7)	57·2 (17·6)	−6·4 (16·1)	124	63·1 (16·6)	63·1 (17·5)	−1·5 (13·7)	−5·5 (−9·2 to −1·7)	0·0040
Generalised anxiety	135	58·6 (16·8)	53·8 (15·1)	−5·3 (13·7)	124	58·5 (16·1)	58·2 (16·6)	−1·6 (13·6)	−3·8 (−7·1 to −0·4)	0·030
Obsessions or compulsions	135	53·3 (12·3)	51·1 (12·4)	−2·0 (12·9)	124	54·2 (13·0)	54·5 (13·1)	−1·2 (13·9)	−2·6 (−5·7 to 0·4)	0·090
Panic	135	63·9 (21·1)	59·8 (22·1)	−3·9 (21·5)	124	64·1 (22·3)	65·3 (22·7)	0·0 (23·4)	−4·7 (−10·3 to 0·8)	0·090
Separation anxiety	135	68·2 (19·9)	59·9 (18·0)	−9·3 (17·9)	124	70·0 (20·9)	67·8 (20·6)	−2·0 (17·4)	−7·8 (−11·6 to −4·1)	<0·0001
Social phobia	135	57·6 (18·6)	53·6 (17·5)	−4·3 (15·2)	124	56·1 (17·0)	56·8 (17·5)	−1·0 (12·5)	−3·28 (−6·6 to 0·1)	0·060
PHQ-9	132	6·5 (5·8)	6·6 (5·3)	0·4 (5·2)	123	7·1 (6·0)	7·7 (6·1)	0·7 (5·9)	−0·7 (−1·9 to 0·5)	0·26
GAD-7	132	7·3 (5·8)	6·5 (5·1)	−0·4 (4·9)	123	7·2 (5·5)	7·9 (5·7)	0·5 (5·8)	−1·1 (−2·2 to 0·03)	0·060

Data are mean (SD) or mean (95% CI), unless otherwise specified. MICE=Mental Health Intervention for Children with Epilepsy. SDQ=Strengths and Difficulties Questionnaire. PedsQL=Paediatric Quality of Life Epilepsy Module. RCADS=Revised Child Anxiety and Depression Scale. PHQ-9=Patient Health Questionnaire. GAD-7=Generalised Anxiety Disorder Assessment. *Data from 72 MICE and 67 control participants who reported having a seizure at baseline and at 12 months post-randomisation.

Table 5: **Adjusted difference in secondary outcome scores between MICE and control groups at baseline and 6 months post-randomisation**

Audiotapes of 251 sessions were selected at random. The overall adherence percentage ranged from 64% to 100% (M=92% [SD 9]). Most sessions contained expected content from the MICE protocol (91%) and therapists did not report delivering any additional content outside of the MICE treatment protocol in any session. The main adaptations were expected changes in focus due to interference (eg, introduction of new material from the protocol due to caregiver mental health). All the audiotapes met the threshold for competence. The total percentage scores on the CTS-R ranged between 50% and 85% (M=60% [SD 7]). Audiotapes of 30 sessions were double rated and there was full agreement with the second rater.

11% of patients experienced at least one serious adverse event, including 14 (8%) of 166 in the MICE group versus 24 (14%) of 168 in the control group (appendix p 11). There was a total of 74 serious adverse events, which were mostly admission due to seizures (50 [68%] of 74).

There were no interactions between the effect of MICE and any of the pre-specified subgroup factors, intellectual disability, autism spectrum disorder, gender, and primary mental health disorder, at 12 months (figure 4). The effect of treatment on SDQ scores was not modified by patient's age, the level of severity of seizures, or by caregiver's level of depression or anxiety, at baseline.

Discussion

Consistent with our hypothesis, MICE was superior to assessment-enhanced usual care in improving emotional and behavioural symptoms in young people with epilepsy and common mental health difficulties, producing a small to moderate between-group effect size of 0·3 at 6 months post-randomisation, which increased to 0·4 at 12 months post-randomisation. These two SDQ points between the MICE and control groups are consistent with the effect sizes found in the previous MATCH-ADTC trial[17] and corresponds to a number needed to

treat of between four and six. Additionally, previous research indicates that the odds of psychiatric disorder decrease by 40% for each 2-point decrease in the parent-reported SDQ.[25] This suggests that MICE had a meaningful and significant clinical effect, which is supported by the parallel effect on children's ability to function as indicated by decreases in the SDQ Impact Scores, as well RCADS scores. Importantly, those with intellectual disability, autism, and with different primary mental health disorders all demonstrated improvement in SDQ scores. This indicates that MICE can be used for many of the children and young people with common mental health difficulties seen by epilepsy services.

The control group also showed some improvement in mental health symptoms, suggesting potential benefit from comprehensive assessment alone. Although this could be due to statistical effects, such as regression to the mean, the control group used more mental health services

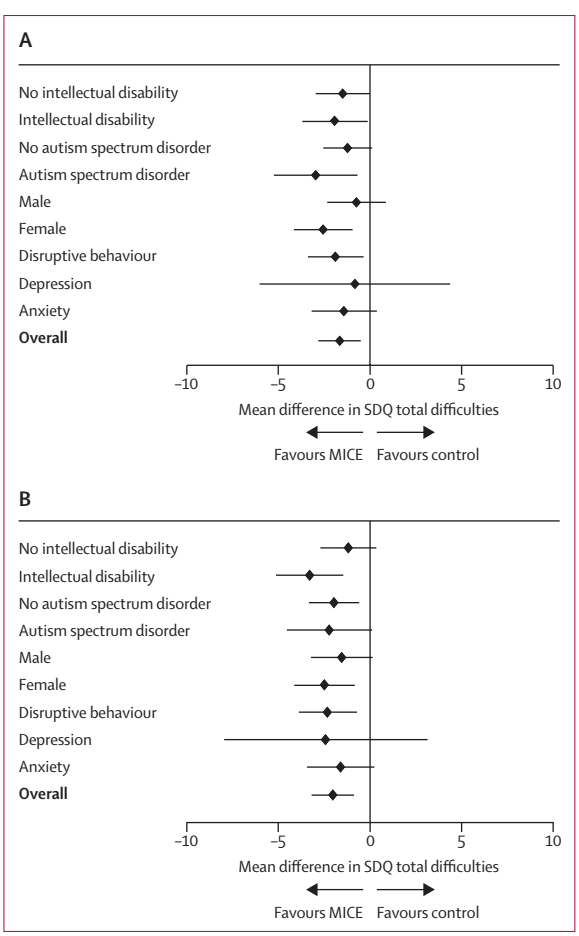

Figure 4: **Effect of MICE on SDQ total difficulties scores, in each subgroup at 6 months (A) and 12 months (B)**

Data are mean difference (95% CI). The pre-registered statistical analysis plan also included subgroup analysis with age dichotomised as younger than 11 years and 11 years and older. This analysis was changed to include age as a continuous variable, which was considered more clinically meaningful. MICE=Mental Health Intervention for Children with Epilepsy. SDQ=Strengths and Difficulties Questionnaire.

than did the MICE group, particularly in the 6–12-month follow-up period. This suggests that taking part in the trial initiated external mental health service use or referrals, perhaps due to a focus on the patient's care generally as they are taking part in a trial, a focus specifically on their mental health, or as a direct result of the assessment report provided to all trial participants and their clinical team.

MICE was also superior to control in improving caregivers' mental health at 6 months post-randomisation, which is important given the known associations with child mental health[26] and poorer physical health and mental health outcomes for caregivers of young people with chronic health conditions,[6,27,28] as well as the consequences of poor mental health in adults.[29] Specifically, depression and anxiety levels, as measured by PHQ-9 and GAD-7, in caregivers in the MICE group improved at 6 months post-randomisation, while they deteriorated among caregivers of patients in the control group. Caregivers might feel less supported if mental health needs are identified for their child but they are not able to access treatments. This might also relate to the additional burden of having to arrange mental health care for their children, again highlighting the value of an integrated service.

Together, the results show a greater benefit of the MICE intervention than the assessment-enhanced usual care. We observed that many staff from within the physical health-care service were keen to take on this service because it gave them tools to address the mental health problems with which their patients frequently presented. The MICE intervention is now being implemented across England.

This trial has several strengths. It is the first full-scale trial of integrated and co-located mental health care in young people with epilepsy, and the first to use a modular psychological approach in young people with chronic health conditions. It demonstrates the possibility of training non-mental health specialists in a flexible cognitive behavioural intervention that can be applied successfully across ages, difficulties, and in the presence of autism spectrum disorder and intellectual disability. Treatment gains were maintained at the 12-month timepoint. The remote delivery enabled participants living in remote locations to participate, minimised travel disruption, and also allowed the trial to recruit and run throughout the COVID-19 pandemic.

The pandemic might have affected participants' mental health; however, this was true for participants in both trial groups. The pandemic might have also affected usual care; hospital visits were cancelled or rescheduled, particularly during the first UK lockdown (March 23–May 10, 2020), and therefore might have caused a reduction in usual care activities. Most of the epilepsy clinics that participants were recruited from moved from in-person to remote (ie, using telephone or video calls) during the lockdowns, and this meant that screening in clinics was reduced and the research was

more reliant on clinician referral. This might have affected the characteristics of participants recruited into the trial (for example, clinicians might have been more likely to identify behavioural difficulties rather than low mood or anxiety). There was no active treatment control group. Caregiver-reported measures were collected due to the age range and high rates of intellectual disability; it is possible that youth-reported measures might have improved identification of internalising disorders.[30] Further research to investigate the effect of MICE on self-reported symptoms among young people would be valuable.

The secondary measures were also not validated across the full age range of the study (eg, the RCADS is validated for those between the ages of 8 years and 18 years). Finally, intellectual disability and autism were reported by caregivers, and no formal measures were used.

In summary, MICE demonstrated significant positive results for young people with epilepsy and their caregivers, which were maintained at 12 months post-randomisation, showing the benefits of integrated physical and mental health care. Non-mental health specialists delivered the treatment, with positive results. The modular nature of the MICE intervention allowed for treatment of co-occurring common mental health difficulties and allowed flexibility in delivery of the protocol so that a wide range of young people, reflecting those seen in clinical practice, were able to benefit from the intervention. This included a diverse population of youth, aged from 3 to 18 years, including those with neurodevelopmental disorders. The strong evidence from this trial suggests that such a model should be fully embedded in epilepsy services and serves as a model for other chronic health conditions in young people. The model is highly consistent with global priorities and action plans. Future research should consider the most effective methods of implementation of this integrated model of care, in both high-resource and low-resource settings.

Contributors

SDB, RS, JHC, and IH conceived the idea for the study with RS and JHC being Chief Investigators and SDB serving as operational lead and primary clinical supervisor. Together with AEC, ED, SB, BC, PF, RM-M, CR, JAS, TS, and SV, they submitted the successful grant application. AEC led on competence and adherence to the protocol. TF was the workpackage lead. SB, RS, and KC drafted the manuscript. KC did the statistical analyses for the manuscript. ED was the patient and public involvement lead. JB was the project manager. HQ was the trial manager. JB, HQ, and KC accessed and verified the data. LX supported the drafting of the manuscript. TH, AL, EM, FW, EW, AD'O, MS, LX, AW, and AZ were research assistants on the study. AV had oversight of the description of the epilepsy diagnoses, KM clinically rated the Development and Wellbeing Assessments, IEN ensured consistency across qualitative and quantitative workpackages, and PG is the junior health economist and ensured consistency with the statistical analyses. All authors had full access to all the data in the study, had final responsibility for the decision to submit for publication, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of interests

JB was funded in part by the National Institute for Health and Care Research (NIHR) Programme Grants for Applied Research (PGfAR) to work on the MICE project in his substantive employment as a Clinical Project Manager at the UCL Comprehensive Clinical Trials Unit. RM-M and SV were funded by NIHR PGfAR. RS was funded by NIHR PGfAR with payment going to UCL for her time on the project. SB was funded by NIHR PGfAR with payments made to her institution King's College London. SDB was funded by NIHR PGfAR to work on the MICE project in her substantive employment as Principal Research Fellow at UCL. BC has received grants from the William T Grant Foundation, Wellcome Trust, and National Institute of Mental Health as principal investigator or co-principal investigator. JHC has received grants from Stoke Therapeutics, Ultragenyx, NIHR, Great Ormond Street Hospital Children's Charity, LifeARC, Waterloo Foundation, and Action Medical Research. SDB has received grants from Epilepsy Research UK and NIHR PGfAR. SV has received grants from the NIHR. RM-M has received grants from MS Society, Crohn's and Colitis UK, and NIHR. BC receives royalties from MATCH-ADTC. PF receives royalties from books with Guildford Press, American Psychiatric Publishing, Oxford University Press. SDB and RS receive royalties from Oxford University Press. RM-M is a beneficiary of license between King's College London and Mahana Therapeutics and has received consulting fees from Mahana Therapeutics and 11 London. PF's honoraria payments for lectures, presentations, and workshops are sent to the Anna Freud centre and he does not receive direct payment for them. JHC's honoraria payments from Biocodex, Nutricia, Jazz Pharmaceuticals, Takeda, and UCB are sent to UCL. SV's honoraria payments from LivaNova for speaking engagements are sent to Great Ormond Street Hospital. RM-M has received payment or honoraria from the European Association of Psychosomatic Medicine, British Association for Behavioural and Cognitive Psychotherapies, and Central and North West London NAtional Health Service (NHS) Foundation Trust. BC received support for attending the OMNI Inventive Care Omaha conference, a children's mental health gathering. TS was reimbursed for travel costs to the annual Royal College of Paediatrics & Child Health Meeting attending to present trial findings. RM-M has received support for attending meetings and for travel from the American Psychosomatic Society, European Association of Psychosomatic Medicine, and British Association for Behavioural and Cognitive Psychotherapies. JHC does not receive personal remuneration for participation in data safety and monitoring boards for Stoke Therapeutics. SV's remuneration for participation in data safety and monitoring boards for advisory board participation from Biocodex is sent to GOSH. BC is a board member of PracticeWise, which owns the MATCH-ADTC protocol on which the Mental Health Intervention for Children with Epilepsy programme is based. PracticeWise was paid for training and consulting during the trial setup phase, and provided supervision of the study supervisors to ensure integrity of treatment implementation. JHC is the Elected President for the International League Against Epilepsy, Chair Medical Board for Matthews Friends, Chair of Medical Board for Dravet UK, Chair of Medical Board for Hope for Hypothalamic Hamartoma, and President of Epilepsy Research UK. PF is Chief Executive of the Anna Freud National Centre for Children and Families, Director for Mental Health and Behaviour Change Programmes for UCLPartners, and National Senior Clinical Advisor for Children and Young People's mental health at NHS England. RS is a director of Bespoke Mental Health. SDB is a psychologist in private practice and a co-director of Mind and Body London. BC did not interact with participants or study therapists and was not involved in the analysis. TS was not involved with the research ethics application for this study. All other authors declare no competing interests.

Data sharing

Data are not publicly available. All requests for data will be reviewed by the Mental Health Intervention for Children with Epilepsy (MICE) study team, to verify whether the request is subject to any intellectual property or confidentiality obligations. Requests for access to the participant-level data from this study can be submitted via email to the corresponding author with detailed proposals for approval. A signed data access agreement with the MICE team is required before accessing shared data. Code is not made available as we have not used custom code or algorithms central to our conclusions.

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