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Brief Communication

Care and three-year outcomes of children with Benign Epilepsy with Centro-Temporal Spikes in England

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ABSTRACT

Purpose: Benign Epilepsy with Centro-Temporal Spikes (BECTS) is a pediatric epilepsy with typically good seizure control. Although BECTS may increase patients' risk of developing neurological comorbidities, their clinical care and short-term outcomes are poorly quantified.
Methods: We retrospectively assessed adherence to National Institute for Health and Care Excellence (NICE) guidelines relating to specialist referral, electroencephalogram (EEG) conduct and annual review in the care of patients with BECTS, and measured their seizure, neurodevelopmental and learning outcomes at three years post-diagnosis.
Results: Across ten centers in England, we identified 124 patients (74 male) diagnosed with BECTS between 2015 and 2017. Patients had a mean age at diagnosis of 8.0 (95% CI = 7.6–8.4) years. 24/95 (25%) patients were seen by a specialist within two weeks of presentation; 59/100 (59%) received an EEG within two weeks of request; and 59/114 (52%) were reviewed annually. At three years post-diagnosis, 32/114 (28%) experienced ongoing seizures; 26/114 (23%) had reported poor school progress;

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15/114 (13%) were diagnosed with a neurodevelopmental disorder (six autism spectrum disorder, six attention-deficit/hyperactivity disorder); and 10/114 (8.8%) were diagnosed with a learning difficulty (three processing deficit, three dyslexia). Center-level random effects models estimated neurodevelopmental diagnoses in 9% (95% CI: 2–16%) of patients and learning difficulty diagnoses in 7% (95% CI: 2–12%).

Conclusions: In this multicenter work, we found variable adherence to NICE guidelines in the care of patients with BECTS and identified a notable level of neurological comorbidity. Patients with BECTS may benefit from enhanced cognitive and behavioral assessment and monitoring.

1. Introduction

Benign Epilepsy with Centro-Temporal Spikes (BECTS), also known as Self-limited Epilepsy with Centro-Temporal Spikes (SeLECTS) or Benign Rolandic Epilepsy has an incidence of ~5/100,000 children and accounts for 10–15% of pediatric epilepsy cases [1]. Patients present at 6–10 years of age with hemifacial motor seizures and associated somatosensory features.

Most patients experience 2–10 seizures during childhood, which usually resolve by adulthood [2]. Despite this, studies have identified cognitive, behavioral, and neurodevelopmental deficits in patients with BECTS [3,4]. An estimated 15–30% of children with BECTS experience neuropsychological impairment, and although general intellectual function is typically normal, abnormalities tend to arise in specific cognitive and behavioral domains [5]. These include language and verbal outcomes, attention, aggression, anxiety, and depression [6,7]. A meta-analysis of literacy and language in children with BECTS identified moderate-to-large mean group differences in single-word reading, receptive and expressive language, and phonological processing when compared with healthy controls [8]. This study reported the importance of early reading and language assessments in children with BECTS.

In addition, studies suggest that patients with BECTS are diagnosed with neurodevelopmental disorders, such as attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD), at higher rates than controls [9]. However, estimates vary widely, many of these studies are cross-sectional rather than longitudinal, and much of this work focusses on individual comorbidities rather than generalized outcomes among patients with BECTS.

Therefore, the proportion of patients with BECTS and comorbid neurodevelopmental disorders and learning difficulties is unclear. Importantly, the previously held view of BECTS as a benign condition may have implications for clinical practice. In addition, many studies on the clinical course of BECTS have been performed in small and single-center populations. To this end, we assessed the care and outcomes of patients in their first three years after a BECTS diagnosis across centers in England. Specifically, we 1) measured adherence to key quality statements (QSs) set by the National Institute for Health and Care Excellence (NICE), and 2) quantified the short-term seizure, learning, and neurodevelopmental outcomes of these patients [10].

2. Material and methods

We retrospectively assessed the care and outcomes of patients diagnosed with BECTS from January 1, 2015 to December 31, 2017 in their first three years post-diagnosis. We included all eligible patients who were diagnosed with BECTS by a consultant pediatric neurologist or pediatrician with specialist interest in epilepsy and were under their care at a secondary or tertiary center in England. Pre-determined exclusion criteria were: 1) patients under the age of two or over the age of 16 at the time of BECTS diagnosis; and 2) patients subsequently diagnosed with a different form of epilepsy. Patients were identified from electroencephalogram (EEG) lists and eligibility was assessed by review of health records. Electronic health records from the first three years post-diagnosis were reviewed.

Clinical data was collected using a pre-defined, standardized collection tool (Table S1). We measured adherence to the following NICE QSs for "Epilepsy in children and young people" (2013):

- QS1: People with a suspected seizure are seen by an epilepsy specialist within two weeks of presentation;
- QS2: Epilepsy investigations (e.g. EEG) are conducted within four weeks of request;
- QS3: Magnetic resonance imaging (MRI) is not indicated in patients with BECTS;
- QS8: Patients with epilepsy undergo an annual review with an epilepsy specialist [10].

Patient outcomes at three years post-diagnosis included seizure frequency, school progress, and neurodevelopmental disorder and learning difficulty diagnoses. These outcome measures were obtained from electronic health records and will have been based on a combination of direct clinical assessment and caregiver/patient self-reporting. Seizure frequencies were recorded as daily, 2–4/week, 1/week, 1–2/month, 2–4/year, 1/year, or <1/year. Participating centers obtained audit approval to allow for local data collection and storage. Descriptive statistics were shared between centers. This work was coordinated through the Neurology and Neurosurgery Interest Group (NANSIG), a UK-wide collaborative for students and junior doctors interested in the clinical neurosciences.

Means (95% confidence intervals [CIs]) are presented for parametric data and medians (interquartile ranges [IQRs]) are presented for non-parametric data. We used center-level random effects models to estimate the prevalence of neurodevelopmental disorder and learning difficulty diagnoses among patients with BECTS within three years of diagnosis. Patients with incomplete follow-up information at three years (for example, due to discharge from routine follow-up, or missing data) were retained in outcome denominators. This was done to avoid overestimating the proportion of patients with a certain outcome at three years post-diagnosis. Data analysis was conducted in RStudio (V2022.7.0.548, RStudio Team, 2020, Boston, MA).

3. Results

3.1. Baseline characteristics

One hundred twenty-four patients (74 male, 60%) were diagnosed with BECTS at ten participating centers in England from 2015 to 2017. The median number of patients per center was ten (IQR = 8–16). The mean age at first seizure was 6.9 (95% CI = 6.5–7.4) years and at diagnosis was 8.0 (95% CI = 7.6–8.4) years (Fig. 1a, b). Of patients with seizure frequencies recorded at

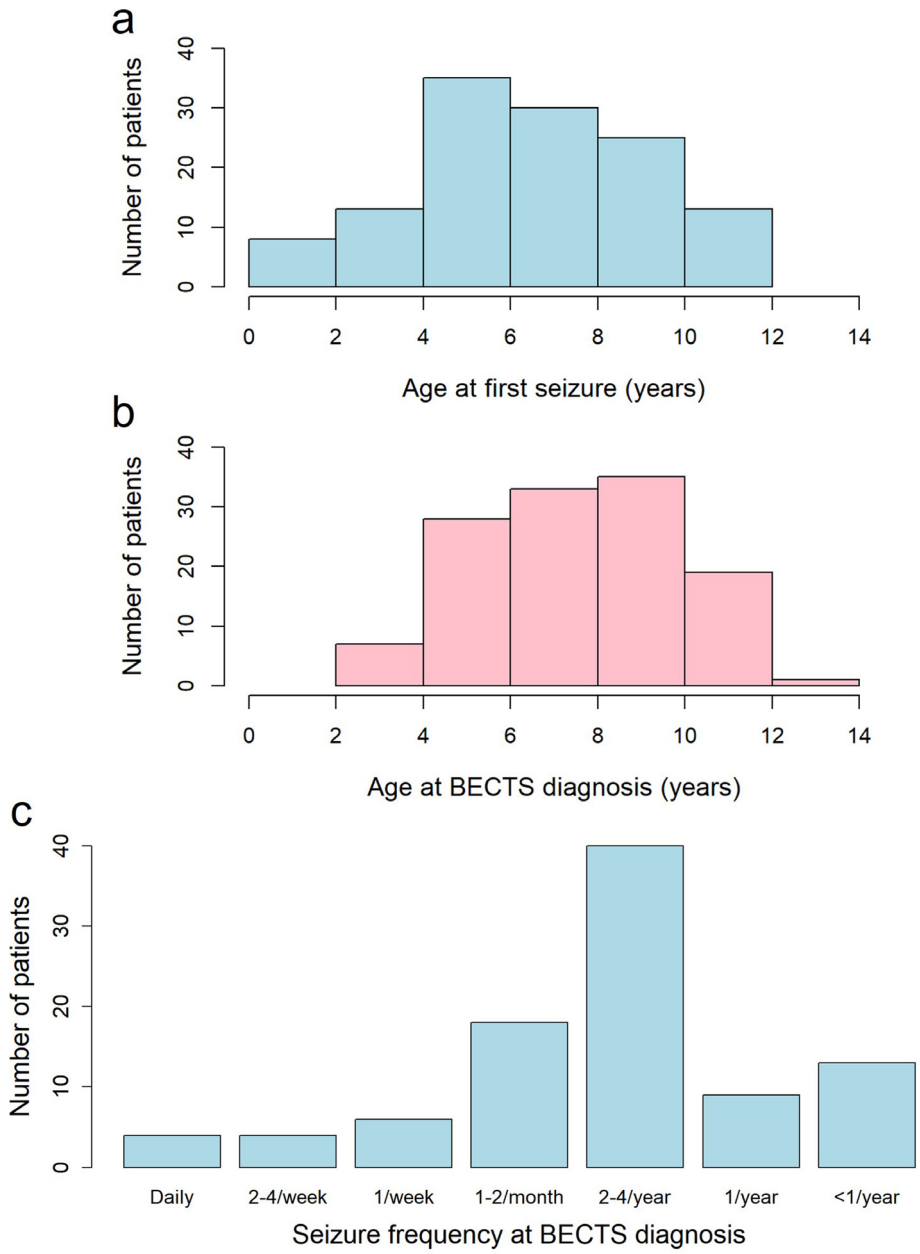


Fig. 1. Baseline clinical characteristics of patients with BECTS. a) Age at time of first seizure (n = 124). b) Age at time of BECTS diagnosis (n = 123). c) Seizure frequency at BECTS diagnosis (n = 94).

presentation, patients experienced 2–4/year (40/94, 43%), ≤1/year (22/94, 23%), 1–2/month (18/94, 19%), 1/week (6/94, 6%), 2–4/week (4/94, 4%), or daily seizures (4/94, 4%) (Fig. 1c). Forty-one out of 94 (44%) patients had bilateral EEG abnormalities, 30/94 (32%) had right unilateral abnormalities, and 23/94 (24%) had left unilateral abnormalities. Seventy out of 122 (57%) patients were prescribed an anti-seizure medication at some point during their care.

3.2. Quality statements

Twenty-four out of 95 (25%) patients were seen by an epilepsy specialist within two weeks of presentation (median = 6.7 weeks, IQR = 2–17) (Fig. 2a, red line denotes QS1), which varied between centers (Fig. 2b). Fifty-nine out of 100 (59%) patients received an EEG within four weeks of request (median = 3.6 weeks, IQR = 1–5) (Fig. 2c, red line denotes QS2). EEG waits also varied between centers (Fig. 2d). 55/123 (45%) patients received an MRI scan (QS3). Nine centers provided three-year follow-up data, at which 59/114 (52%) patients were reviewed annually by an epilepsy specialist (Fig. 2e, QS8).

3.3. Outcomes at three years post-diagnosis

One center (ten patients) did not provide outcome data at three years post-diagnosis. Across nine centers, at three years post-diagnosis, 32/114 (28%) patients experienced ongoing seizures (Fig. 3a). Of patients with ongoing seizures at three years post-diagnosis and data available (20/32 [63%]), 6/20 (30%) patients experienced 1/year; 6/20 (30%) experienced 2–4/year; 3/20 (15%) experienced 6–10/year; 3/20 (15%) experienced 1–2/month; 1/20 (5%) experienced 1/week; and 1/20 (5%) experienced daily seizures.

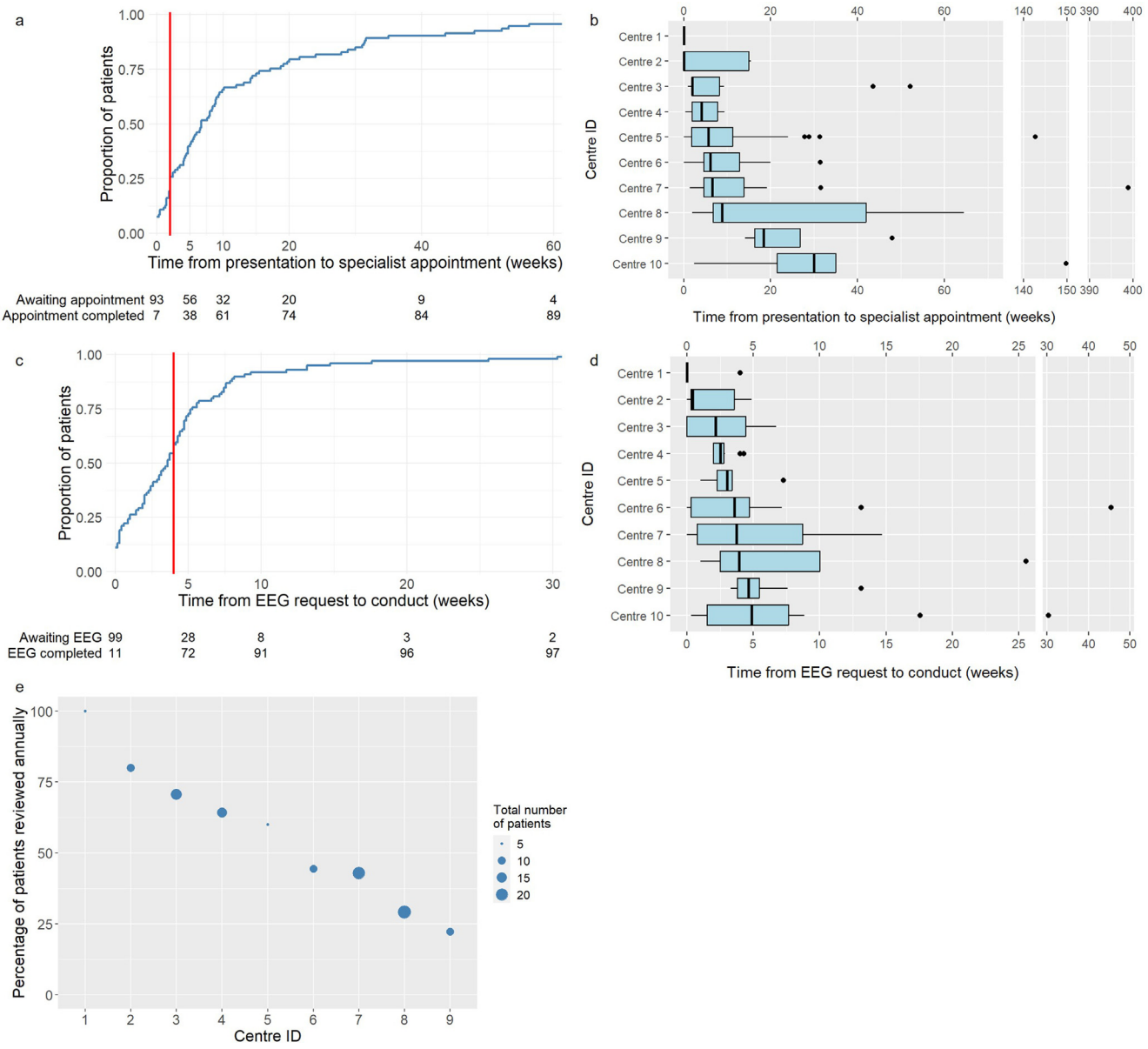
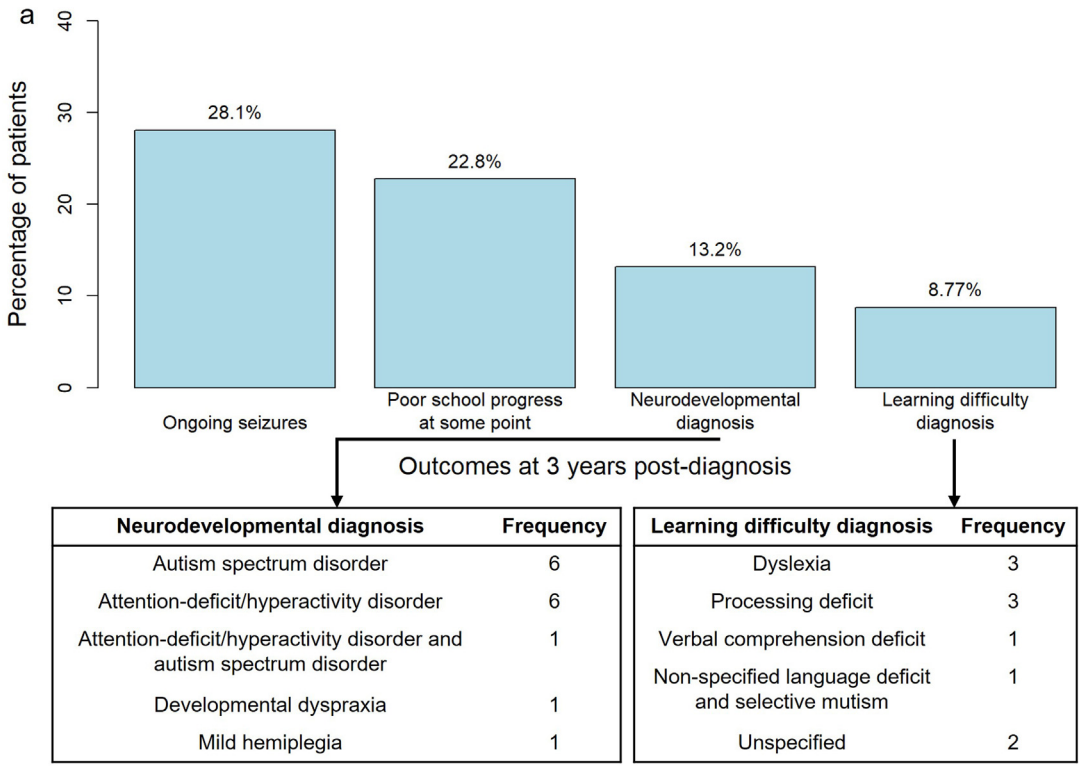


Fig. 2. Adherence to NICE quality statements 1, 2 and 8 in the care of patients with BECTS. a–b) Time from presentation to an appointment with an epilepsy specialist (n = 93). c–d) Time from electroencephalogram request to conduct (n = 99). e) Percentage of patients reviewed annually by an epilepsy specialist (n = 114). Vertical red lines in a and c denote NICE quality statements 1 and 2, respectively. To avoid center identification, center numbers in 1b, d and e do not necessarily correspond.

Twenty-six out of 114 (23%) patients reported poor school progress at some point during their care. Fifteen out of 114 (13%) patients were diagnosed with a neurodevelopmental disorder (six ASD, six ADHD, one ASD and ADHD, one developmental dyspraxia, one mild hemiplegia). Notably, in most cases (9/15, 60%), these neurodevelopmental diagnoses were made before or at the time of BECTS diagnosis. Ten out of 114 (8.8%) patients were diagnosed with a learning difficulty (three processing deficit, three dyslexia, one verbal comprehension deficit, one unspecified language deficit and selective mutism, two unspecified). Most commonly (7/10, 70%), learning difficulties were also diagnosed prior or simultaneously to BECTS. Center-level random effects models estimated neurodevelopmental diagnoses in 9% (95% CI: 2–16%) of patients and learning difficulty diagnoses in 7% (95% CI: 2–12%) (Fig. 3b, c).

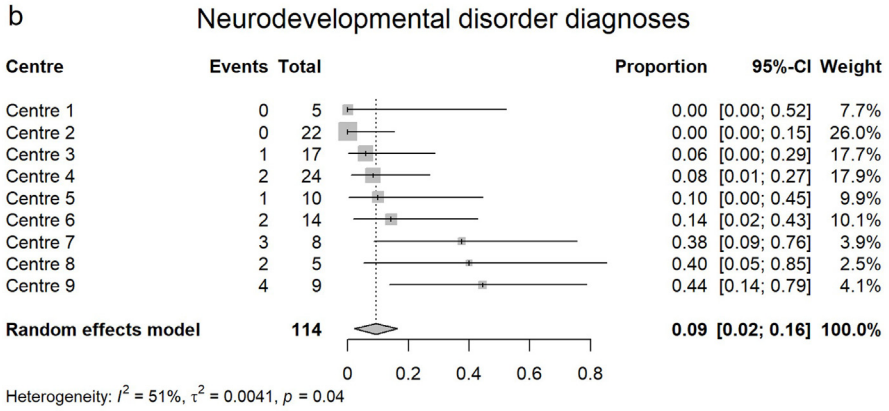
4. Discussion

We identified variable adherence to NICE guidelines relating to specialist appointments, EEG and MRI conduct, and annual review in the care of patients with BECTS. A significant proportion of patients (~30%) experienced ongoing seizures three years post-diagnosis and/or reported difficulties at school. A smaller percentage of patients (~15%) were diagnosed with a neurodevelopmental and/or learning comorbidity. These findings support the International League Against Epilepsy's reclassification of BECTS to SeLECTS, because patients may experience neurological comorbidities despite having self-limiting seizures [11]. This suggests that some patients with BECTS may benefit from enhanced assessment and monitoring.



Neurodevelopmental diagnosis	Frequency
Autism spectrum disorder	6
Attention-deficit/hyperactivity disorder	6
Attention-deficit/hyperactivity disorder and autism spectrum disorder	1
Developmental dyspraxia	1
Mild hemiplegia	1

Learning difficulty diagnosis	Frequency
Dyslexia	3
Processing deficit	3
Verbal comprehension deficit	1
Non-specified language deficit and selective mutism	1
Unspecified	2



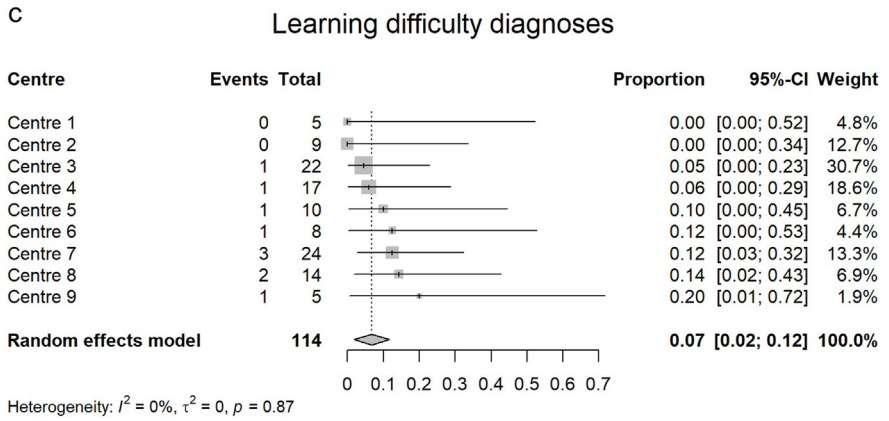


Fig. 3. Outcomes of patients with BECTS at three years post-diagnosis. a) Proportion of patients with ongoing seizures, poor school progress, a neurodevelopmental disorder or a learning difficulty (n = 114). b–c) Center-level random effects models of patients diagnosed with a neurodevelopmental disorder or learning difficulty (n = 114). To avoid center identification, center numbers in 2b and c do not necessarily correspond.

The delays in specialist appointments (25% within two weeks) and EEG conduct (59% within four weeks) in our cohort are similar to those identified by the Epilepsy12 national audit of all newly-diagnosed pediatric epilepsy patients [12]. Almost half of patients received an MRI scan, despite guidelines recommending to the contrary because patients with BECTS are unlikely to have etiological structural abnormalities [10]. Our data on the proportion of patients receiving an annual review with an epilepsy specialist (52%) have not been described in other forms of epilepsy. These findings identify important areas for quality improvement in the care of patients with BECTS and we encouraged local dissemination of results in participating centers. In particular, we identified significant variation between centers, which reinforces findings of regional inequalities in epilepsy services and care [12]. Many active programs aim to improve pediatric epilepsy care in England, which is highly encouraging.

Previous work has identified deficits in specific cognitive domains, such as executive and language functions, amongst patients with BECTS, even when IQ is normal [6,13–15]. One outstanding question from these studies and our work is whether there are subgroups of patients with BECTS who are at increased risk of experiencing seizures throughout puberty and/or of developing neurological comorbidities. A younger age of seizure onset, more so than duration of epilepsy, may increase patients' risk of developing cognitive deficits [13,15,16]. The laterality of EEG abnormalities in patients with BECTS does not seem to be associated with cognitive or behavioral outcomes, although it has been suggested that extrarolandic and other atypical features may be more common in patients with neurological comorbidities [2]. Frequent centro-temporal spikes during sleep may also mediate neurological outcomes [16]. We were unable to study these putative associations further because patient-level data was not shared between centers due to data sharing constraints. The long-term neurodevelopmental and cognitive outcomes of patients with BECTS also warrant further study.

Notably, most patients in our cohort who were diagnosed with a neurodevelopmental disorder or learning difficulty received their diagnosis prior or simultaneously to BECTS. This is in line with previous reports and provides some mechanistic insight into patients' neurological comorbidities [17]. This may suggest that the pre-clinical stages of BECTS are underrecognized, which would reinforce the importance of a timely epilepsy referral and diagnosis.

Our multicenter approach provides a large sample of consecutive patients and allows us to form a meaningful snapshot of clinical practice. Our primary data collection method also records information which is not always available in registries. However, there are also some limitations. First, we mostly included tertiary care settings, and given that many patients with BECTS are seen in district general hospitals, this may have selected for patients with more complex disease courses. However, the characteristics of our cohort, including male/female ratio, age of diagnosis, and seizure frequency are comparable to those of other studies using different patient identification methodologies [18,19]. Second, our retrospective use of electronic health records means our findings are limited by the completeness of clinical documentation and associated reporting biases. This includes variation within and between centers in how clinicians will have asked patients and caregivers about seizures, school progress, and comorbid diagnoses. In addition, we did not record objective measures of the severity of patients' neurodevelopmental disorder and learning difficulty diagnoses, which may have provided further insight into these associations and their temporal trends. Finally, we did not include a control group, such as age-matched healthy controls or patients with another form of epilepsy, which would have helped describe the specificity of these findings to patients with BECTS.

5. Conclusions

We identify variable adherence to NICE guidelines relating to specialist appointments, EEG and MRI conduct, and annual review in the care of patients with BECTS. Twenty-eight percent of patients experienced ongoing seizures three years post-diagnosis and neurodevelopmental disorders and learning difficulties were each diagnosed in ~10% of patients. Patients with BECTS may benefit from enhanced cognitive and behavioral assessment and monitoring.

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Data availability statement

Summative statistics from centers will be made available upon reasonable request to Moritz Steinruecke.

CRediT authorship contribution statement

Moritz Steinruecke: Conceptualization, Methodology, Investigation, Formal analysis, Visualization, Writing – review & editing, Writing – original draft. **Conor Gillespie:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing. **Najma Ahmed:** Investigation, Formal analysis, Writing – review & editing. **Soham Bandyopadhyay:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Dorota Duklas:** Investigation, Formal analysis, Writing – review & editing. **Mahta Haghighat Ghahfarokhi:** Investigation, Formal analysis, Writing – review & editing. **David E Henshall:** Conceptualization, Methodology, Visualization, Writing – review & editing, Writing – original draft. **Mehdi Khan:** Investigation, Formal analysis, Writing – review & editing. **Rosaline de Koning:** Investigation, Formal analysis, Writing – review & editing. **James Madden:** Investigation, Formal analysis, Writing – review & editing. **Jeffery Samuel Nicholas Marston:** Investigation, Formal analysis, Writing – review & editing. **Rana Ali Abdelrahim Mohamed:** Investigation, Formal analysis, Writing – review & editing. **Shiva A Nischal:** Investigation, Formal analysis, Writing – review & editing. **Emma Jane Norton:** Investigation, Formal analysis, Writing – review & editing. **Gokul Parameswaran:** Investigation, Formal analysis, Writing – review & editing. **Anca-Mihaela Vasilica:** Investigation, Formal analysis, Writing – review & editing. **John Ong Ying Wei:** Investigation, Formal analysis, Writing – review & editing. **Chloe EC Williams:** Investigation, Formal analysis, Writing – review & editing. **Ffion Williams:** Investigation, Formal analysis, Writing – review & editing. **Shakti Agrawal:** Investigation, Writing – review & editing, Supervision. **Dionysios N Grigoratos:** Investigation, Writing – review & editing, Supervision. **Anil Israni:** Investigation, Writing – review & editing, Supervision. **Ram Kumar:** Investigation, Writing – review & editing, Supervision. **Nadine McCrea:** Investigation, Writing – review & editing, Supervision. **Jayesh Patel:** Investigation, Writing – review & editing, Supervision. **Maria-Christina Petropoulos:** Investigation, Writing – review & editing, Supervision. **Jaspal Singh:** Investigation, Writing – review & editing, Supervision.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing

interests: Shakti Agrawal has had speaking contracts with USB Medical, GW Pharmaceuticals and Nutricia. The remaining authors have no conflicts of interest to report.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2023.109465.

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