IMPORTANCE  Children with benign epilepsy with centrotemporal spikes (BECTS) have traditionally been considered to have a uniformly good prognosis. However, *benign* may be a misnomer because BECTS is linked to cognitive deficits, a more severe phenotype with intractable seizures, and the potential for sudden unexpected death in epilepsy (SUDEP).

OBJECTIVE  To determine if cases of BECTS are present in the North American SUDEP Registry (NASR).

DESIGN, SETTING, AND PARTICIPANTS  The NASR is a clinical and biospecimen repository established in 2011 to promote SUDEP research. The NASR database, which includes medical records, results of electroencephalographic tests, and interviews with family members of patients with epilepsy who died suddenly without other identifiable causes of death, was queried from June 3, 2011, to June 3, 2016, for cases of BECTS. The patients with epilepsy had died suddenly without other identifiable causes of death (eg, drowning, trauma, exposure to toxic substances, or suicide); SUDEP classification was determined by the consensus of 2 epileptologists.

MAIN OUTCOMES AND MEASURES  Cases of SUDEP among children who received a diagnosis of BECTS among patients reported in the NASR.

RESULTS  Three boys (median age at death, 12 years; range, 9-13 years) who received a diagnosis of BECTS by their pediatric epileptologist or neurologists were identified among 189 cases reported in the NASR. The median age of epilepsy onset was 5 years (range, 3-11 years), and the median duration of epilepsy was 4 years (range, 1-10 years). Two deaths were definite SUDEP, and 1 was probable SUDEP. Independent review of clinical and electroencephalographic data supported the diagnosis of BECTS in all 3 patients. None of the patients was prescribed antiseizure drugs, either owing to physician recommendation or mutual decision by the physician and parents. All 3 patients were found dead in circumstances typical of SUDEP. The 3 patients spanned the spectrum of BECTS severity: 1 had only a few seizures, 1 had more than 30 focal motor seizures, and 1 had 4 witnessed generalized tonic-clonic seizures and approximately 30 suspected generalized tonic-clonic seizures.

CONCLUSIONS AND RELEVANCE  Sudden unexpected death in epilepsy is a very rare outcome in BECTS that clinicians should consider discussing in appropriate circumstances and possibly factoring into treatment decisions.
Benign epilepsy with centrotemporal spikes (BECTS) is the most common focal epilepsy syndrome among children. Focal motor seizures involving the face, oropharyngeal region, or upper limb are most common, although sensory symptoms involving the mouth can often occur.\(^1\) Half of children with BECTS also have 1 or more generalized tonic-clonic seizures (GTCSs).\(^2\) Seizures in BECTS are usually nocturnal, at the transition of sleep onset or offset. Many neurologists do not prescribe antiseizure drugs because the seizures are infrequent (half of the patients with BECTS have had fewer than 6 seizures 5 years after diagnosis\(^2\)), BECTS resolves before 16 years of age, and it has an excellent prognosis.\(^1\)\(^,\)\(^3\)

Although these children most often outgrow epilepsy and have normal or near-normal adult lives,\(^2\) the term benign belies several features. Compared with healthy controls, children with BECTS score significantly lower on tasks of expressive language, efficiency of verbal learning, and motor and psychomotor speed and dexterity and have significantly higher rates of attention, social, and other behavioral disorders.\(^4\) Furthermore, some patients with BECTS are treatment resistant or have more frequent GTCSs. Given the nocturnal predominance of seizures and the occurrence of GTCSs, patients with BECTS could be at risk of sudden unexpected death in epilepsy (SUDEP), but SUDEP in well-characterized patients with BECTS has not been documented. We report on 3 children with BECTS among a series of cases of SUDEP.

Methods

We searched the records of 189 decedents enrolled in the North American SUDEP Registry (NASR), a clinical and biospecimen repository established to investigate the risk factors and mechanisms for SUDEP (http://sudepregistry.org), from June 3, 2011, to June 3, 2016. Cases were identified based on a diagnosis of BECTS by parental report during the intake interview and confirmed by the treating physicians in the medical records. Diagnostic criteria for BECTS include the following: onset of epilepsy at 3 to 13 years of age, normal cognition and development before onset of seizures, no symptomatic cause of epilepsy, and electroencephalogram (EEG) results reporting discharges consistent with BECTS.\(^1\)\(^,\)\(^5\) Two epileptologists (D.F. and O.D.) independently confirmed and classified\(^6\) SUDEP using interview data and medical records. This study was approved by the New York University School of Medicine Institutional Review Board. All participants provided written informed consent.

Results

We identified 3 children who received a diagnosis of BECTS by pediatric neurologists (patients 1 and 2) and a pediatric epileptologist (patient 3) among the cases of SUDEP reported in the NASR. Patients 1 and 3 met all clinical and EEG features for a diagnosis of BECTS (Table). Patient 2 had limited EEG data (a 27-minute study showed 2 spikes over F3/C3) but had classic clinical features of BECTS.

All 3 patients were male, with a median age at death of 12 years (range, 9-13 years). The median age of epilepsy onset was 5 years (range, 3-11 years), and the median duration of epilepsy was 4 years (range, 1-10 years). Two patients experienced nocturnal GTCSs. None of the 3 children was treated with antiseizure drugs, per physician recommendation in 2 patients and mutual decision by the physician and parents in 1 patient. None of the families was counseled about the risk of SUDEP.

Report of Cases

Case 1

A 9-year-old boy had seizure onset at 5 years of age. Within a few hours of sleep, he awoke with unilateral numbness of the face and tongue, affecting either the left or right side, and he would not speak for several minutes. Recovery was abrupt. He could respond during the seizure and remember what happened during the seizure. His parents witnessed more than 20 of these seizures during 3 years. Within months of seizure onset, he began to have 30- to 60-second GTCSs during sleep or shortly after awakening. These seizures were associated with cyanosis, hypersalivation, and a gurgling noise. After the seizures, he fell back asleep but was described by his mother as “off” in the morning, or, if he was awake, he was confused and lethargic for 20 to 30 minutes. The patient’s parents witnessed 3 to 4 GTCSs but suspected that he had experienced 30 to 50 GTCSs during his lifetime based on his behavior after awakening. He had no risk factors for epilepsy except for a maternal grandmother with focal epilepsy beginning in her 40s. No other family members, including his 3 siblings, had epilepsy. He had a history of asthma treated with cetirizine hydrochloride and fluticasone propionate as needed.

The patient’s pediatric neurologist diagnosed BECTS based on clinical history and EEG results showing bilateral independent central-temporal epileptiform activity. His mother reported that the neurologist recommended not to use antiseizure drugs because the medications were “more harmful than the seizures and since he would outgrow his epilepsy.” He had an increase in the frequency of both focal motor and secondary GTCSs in the 6 months prior to death, with the most recent suspected GTCS occurring 8 to 14 days before death. His mother recalled, “the neurologist said ‘if things got worse,’ we...
should come back, but there was no quantification of what ‘worse’ was. I read on reputable websites that increased seizure activity at his age was common, so I decided this was normal and nothing to worry about, despite the fact I was concerned.”

His death was unwitnessed, although he shared a room with a sibling who slept in another bed. He went to bed around 7:30PM and was found at 6:10AM lying prone in his bed at home with saliva on his face. On parent report, “full rigor mortis” had set in, suggesting death before midnight. Results of a postmortem examination revealed no structural or toxicologic findings; his death was determined to be due to SUDEP.

**Case 2**

A 12-year-old boy developed epilepsy at 11 years of age. His first seizure was a nocturnal focal motor seizure affecting his facial muscles and resulting in speech arrest for less than 2 minutes. There may have been mild upper extremity movements, but there was no loss of consciousness. The patient was referred to a pediatric neurologist at a major academic children’s hospital. He received a clinical diagnosis of BECTS, and no antiseizure drugs were prescribed. Nine months later, while on a family vacation sleeping in the same hotel room, the parents witnessed a GTCS while the patient was sleeping. Results of an EEG subsequently revealed epileptiform activity with rare left frontal central spikes, consistent with Rolandic epilepsy (also known as BECTS). No antiseizure drugs were prescribed, and the parents were reassured that he would likely outgrow the epilepsy.

During the next 4 months, the patient experienced at least 3 additional nocturnal GTCSs. He slept alone and was found dead in the morning in the prone position in bed with urinary incontinence. Cardiopulmonary resuscitation was unsuccessful. The autopsy report listed the cause of death as “cardiac dysrhythmia associated with lymphocytic myocarditis, left anterior descending coronary artery intramural tunneling, and possible hypertrophic cardiomyopathy” (heart weight, 340 g; predicted, 140-300 g). The autopsy report did not mention seizures or epilepsy. Neither adjudicator considered the cardiac findings as an independent cause of death because the myocardiitis was mild and death did not occur during physical activity; the case was determined to be definite SUDEP by both adjudicators independently.

### Table. Clinical Characteristics and Circumstances of Death for Patients With BECTS Enrolled in the NASR

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Age at death, y</td>
<td>9</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td><strong>Medical history</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at onset of epilepsy, y</td>
<td>5</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Focal sensorimotor seizures</td>
<td>Facial twitching (usually near onset of sleep)</td>
<td>Facial muscles and speech arrest</td>
<td>Unilateral face and arm clonic jerking</td>
</tr>
<tr>
<td>Lifetime GTCSs</td>
<td>30-50 Suspected; &lt;5 witnessed (usually)</td>
<td>4</td>
<td>None witnessed; suspected rare GTCSs in sleep based on postictal symptoms</td>
</tr>
<tr>
<td>GTCs in last year</td>
<td>Approximately 20 suspected; &lt;2 witnessed</td>
<td>4</td>
<td>2 suspected</td>
</tr>
<tr>
<td>Nocturnal seizures</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>EEG findings</td>
<td>Bilateral independent central-temporal sharp-slow waves, which increase in sleep</td>
<td>Rare left frontal central spikes</td>
<td>Frequent right central, parietal, and temporal spikes with aftergoing slow waves and right mild temporal focal slowing</td>
</tr>
<tr>
<td>Treatment with antiseizure drugs</td>
<td>No, per physician recommendation</td>
<td>No, per physician recommendation</td>
<td>No, per decision between physician and parents</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Asthma with wheezing and rhinitis</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Circumstances of death</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time found</td>
<td>6:10 AM</td>
<td>6:15 AM</td>
<td>8:00 AM</td>
</tr>
<tr>
<td>Location</td>
<td>Home, in bed</td>
<td>Home, in bed</td>
<td>Home, in bed</td>
</tr>
<tr>
<td>Position</td>
<td>Prone</td>
<td>Prone</td>
<td>Prone</td>
</tr>
<tr>
<td>Evidence of preceding seizure</td>
<td>Saliva on face</td>
<td>Urinary incontinence</td>
<td>Blood on pillow, left upper extremity in abnormal position</td>
</tr>
<tr>
<td>Pathologic findings</td>
<td>Pulmonary edema</td>
<td>Pulmonary edema, heart 340 g (expected upper limit of normal, 300 g), mild subaortic stenosis, mild endocardial fibrosis, foci of lymphocytic myocarditis, dilation of fourth ventricle, subependymal gliosis, and granular ependymitis of fourth ventricle</td>
<td>No autopsy</td>
</tr>
<tr>
<td>Cause of death on autopsy</td>
<td>SUDEP</td>
<td>Cardiac dysrhythmia</td>
<td>No autopsy</td>
</tr>
<tr>
<td>SUDEP discussion between physician and parents</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Abbreviations: BECTS, benign epilepsy with centrotemporal spikes; EEG, electroencephalogram; GTCSs, generalized tonic-clonic seizures; NASR, North American SUDEP Registry; SUDEP, sudden unexpected death in epilepsy.
Sudden Death in Benign Childhood Epilepsy With Centrotemporal Spikes

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Case 3
A 13-year-old boy developed epilepsy at 3 years of age. His first seizure occurred 20 minutes after falling asleep, with left face followed by left arm clonic jerking associated with hypersalivation. An EEG was performed; results showed typical features of BECTS. One year later, the patient had a similar seizure during an afternoon nap. Thereafter, he continued to experience nocturnal focal motor seizures 3 to 4 times per year. The patient was referred to a pediatric epileptologist at an academic medical center who performed an EEG; results described epileptiform discharges in the right central, temporal, and parietal regions and was interpreted by the pediatric epileptologist as consistent with BECTS. The patient’s parents, including his physician father, never witnessed a GTCS but believe, based on the severity of his postictal state, that he had rare GTCSs but probably 2 in the year before he died, which was unusual. A trial of antiseizure drugs was considered by the epileptologist, but, in concert with the parents, it was mutually decided that the medication’s adverse effects likely outweighed the effects of the rare seizures with disabling postictal symptoms.

The patient slept alone and was found dead, lying prone in his bed at home at 8:00 AM. Based on his usual pattern of seizures within 30 minutes after falling asleep and rigor mortis, the estimated time of death was 11:30 PM. He slept alone in a bed in his own room. The death was unwitnessed, but blood on his pillow suggested a nocturnal seizure. An autopsy was not performed.

Discussion
We identified 3 cases of SUDEP in children with BECTS among 189 decedents enrolled in the NASR. The largest study of mortality among children with epilepsy combined 4 published cohorts (2239 patients with >30 000 person-years of follow-up) and found no seizure-associated deaths among children with BECTS.6 Two small epidemiologic studies did not identify SUDEP among patients with BECTS.3,5 Children with uncomplicated or idiopathic epilepsy comprise 9% to 30% of pediatric SUDEP cohorts.6,7 The estimated rate of SUDEP among children with uncomplicated epilepsy was 9 children per 100 000 patient-years.6 One case of SUDEP in a child with BECTS was reported in an autopsy series8 without confirmatory clinical or EEG features. We document SUDEP in 2 children with definite BECTS and 1 with probable BECTS.

The history of multiple witnessed nocturnal focal motor seizures or GTCSs, death in sleep, and the death scene strongly support SUDEP in all 3 patients.9 The death scene revealed evidence of a seizure in sleep, with prone positioning as well as incontinence, drool, or blood on the pillow in each case. For 1 patient, the postmortem examination revealed a slightly hypertrophic heart, but it was thought that this was insufficient to cause death in isolation, although it may have predisposed him to seizure-induced death.

The frequency and severity of seizures in our patients are difficult to precisely define, but they are within the spectrum of BECTS. One patient experienced approximately 30 witnessed or self-reported nocturnal focal motor seizures (face and upper extremity) during a decade. One child had only 4 witnessed GTCSs, but his mother suspected that he had experienced 2 unwitnessed GTCSs per month based on possible postictal symptoms. The final patient had 1 focal motor and 4 GTCSs before his presumed terminal seizure. Five years after diagnosis, typical patients with BECTS have experienced more than 50 seizures (10%), 6 to 50 seizures (45%), and fewer than 6 seizures (45%).2 Among 8 studies, a mean of 62% of children with BECTS experienced at least 1 GTCS.2

Limitations
Typical BECTS carries an extremely low risk of premature mortality. None of our patients had features that identified them as high risk for SUDEP. Patient 1 had 4 witnessed but more than 30 suspected nocturnal GTCSs during 4 years. As with most cases of BECTS, it is impossible to know the exact number of unwitnessed focal seizures or GTCSs. Seizures may go undetected in BECTS because they often occur during the night when caretakers are asleep. None of our patients was taking antiseizure drugs when they died: 2 because of physician recommendation and 1 because of a joint decision between the physician and parents. The decision if and when to treat patients with BECTS is not straightforward. It is uncertain if antiseizure drugs would have prevented SUDEP in any of the patients, although seizure control is considered the most effective way to reduce the risk of SUDEP.9 The frequent adverse effects of antiseizure drugs must be considered. We lack prospective, large sample population-based data but may need to treat 1000 patients with BECTS to possibly prevent 1 case of SUDEP. For those with nocturnal seizures, medications given before bedtime may help reduce daytime adverse effects and help control nocturnal seizures. We lack data on the role of seizure monitors and the prevention of SUDEP, but such monitors may save lives.

Conclusions
The challenge for the clinician is whether to disclose information about risk of SUDEP to the families of patients with BECTS at diagnosis or afterward. Our data suggest that even children with BECTS who have only focal motor or infrequent seizures are at risk for SUDEP. Families are increasingly aware of SUDEP even if the risk is not disclosed by the physician. These cases illustrate that SUDEP is a rare complication of BECTS, and this information should be shared with families at or soon after diagnosis.
for the integrity of the data and the accuracy of the
data analysis.

Study concept and design: Doumlele, Friedman,
Buchhalter, Donner, Devinsky.

Acquisition, analysis, or interpretation of data: All
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Drafting of the manuscript: Doumlele, Friedman,
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Critical revision of the manuscript for important
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Administrative, technical, or material support: Louik.

Study supervision: Doumlele, Friedman, Buchhalter,
Donner, Devinsky.

Conflict of Interest Disclosures: Drs Friedman,
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Additional Contributions: We thank the patients’
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