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Identifying Unrecognized Cases of Lennox-Gastaut Syndrome in Adults With Intellectual Disability in Germany: Data from the Epilepsy Diagnostic Potential Analysis (EpiDIAL) Study

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Introduction

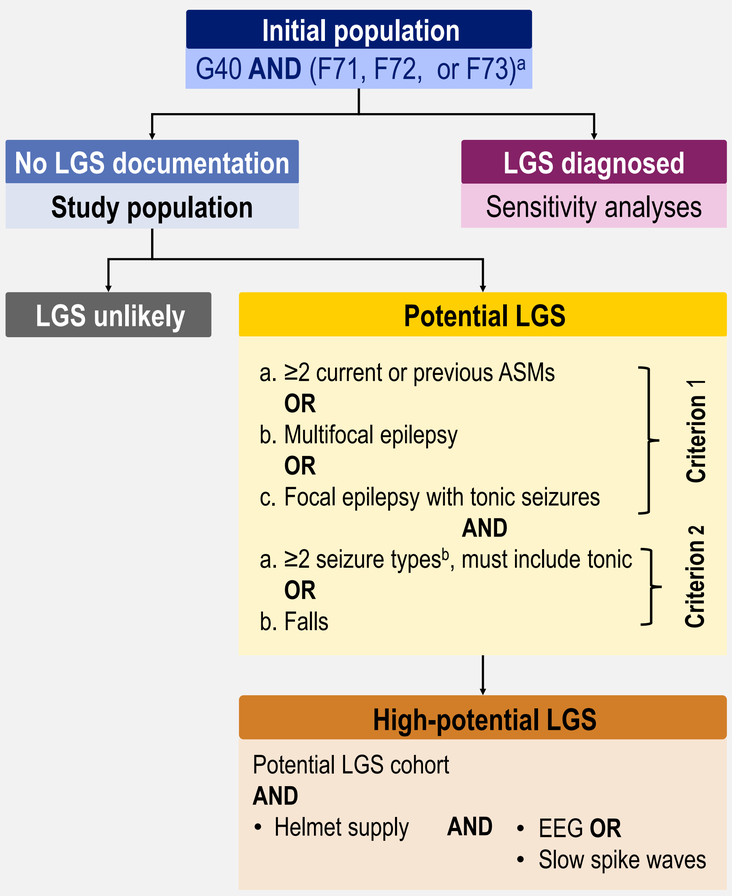
- Lennox-Gastaut syndrome (LGS) is a rare developmental and epileptic encephalopathy characterised by childhood onset of multiple types of treatment-resistant seizures, including tonic seizures, cognitive and often behavioural impairments, distinctive electroencephalogram (EEG), and poor prognosis[1–3]
- LGS is challenging to diagnose, due to its polymorphic and evolving presentation; accurate diagnosis is essential to enable access to appropriate, personalised care[2–5]
- Algorithms to facilitate patient identification, such as REST-LGS, can be helpful in identifying adult patients with the potential of a missing diagnosis of LGS, but a requirement for criteria that may be absent in medical records potentially complicates their use in some real-world settings[5,6]

Objective

- The Epilepsy Diagnostic Potential Analysis (EpiDIAL) study aimed to identify potential undocumented cases of LGS in adults, using patient records from specialised medical centres for adults with disabilities (MZEB) in Germany

Methods

Figure 1. EpiDIAL algorithm to identify undocumented LGS in patient records



[a]Medical records screened for ICD-10-GM codes of epilepsy (G40) AND intellectual disability (F71 [moderate], F72 [severe], or F73 [profound]); [b]Tonic, axial-tonic, absence or atonic seizures.
ASM, antiseizure medication; EEG, electroencephalogram; ICD-10-GM, German Modification of the International Statistical Classification of Diseases, 10th Revision; LGS, Lennox-Gastaut syndrome.

- For this retrospective chart review, we developed an algorithm based on the International League Against Epilepsy criteria,[7] and applied it to patient records that had been screened for documented epilepsy (ICD-10-GM: G40) and intellectual disability diagnoses (F71–F73) (**Figure 1**)

Participating centres (Germany)

Sensitivity analyses

- **Sensitivity analysis 1:** Criterion 2a was amended to: **≥2 seizure types with no obligation of tonic seizure**
- **Sensitivity analysis 2:** Criterion 2a was modified to: **≥3 seizure types with no obligation of tonic seizure**

Results

Table 1. Patient records identified as potential and high-potential LGS

Centres and patient records	Centre 1 (N=75)	Centre 2 (N=121)	Centre 3 (N=135)	Centre 4 (N=81)	Total (N=412)
LGS diagnosed, n	9	20	5	15	49
No LGS documentation (Study population), n	66	101	130	66	363
LGS unlikely, n (%)[a]	44 (67)	87 (86)	75 (58)	29 (44)	235 (65)
Potential LGS, n (%)[a]	22 (33)	14 (14)	55 (42)	37 (56)	128 (35)
High-potential LGS, n (%)[a]	0 (0)	1 (1)	6 (5)	21 (32)	28 (8)

[a]Percentages are calculated from the Study population; Potential LGS also includes the High-potential LGS group. LGS, Lennox-Gastaut syndrome.

- Overall, 412 patient records with consultations between March 2015 and December 2024 across the centres were reviewed (**Table 1**)
  - 49 had documented LGS diagnosis; 363 had no LGS documentation
- Among those with no LGS documentation, 128 (35%) were identified by the EpiDIAL algorithm as 'Potential LGS', including 28 (8%) identified as 'High-potential LGS'

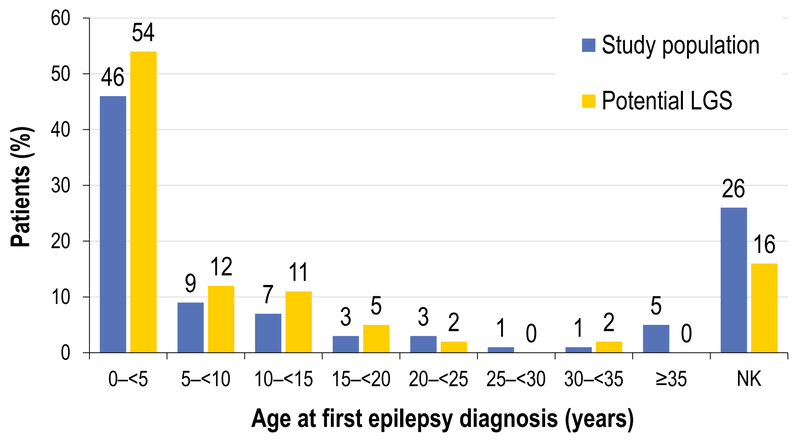
Table 2. Patient characteristics

	LGS diagnosed (n=49)	LGS unlikely (n=235)	Potential LGS (n=128)	High-potential LGS (n=28)	Total (N=412)
Age at first presentation in MZEB, years, mean	29.7	34.2	29.2	33.3	31.8
Treatment duration in MZEB, years, mean (median)[a]	3.0 (3)	3.0 (3)	3.1 (3)	3.7 (4)	NA
Male, n (%)	29 (59)	131 (56)	75 (59)	18 (64)	235 (57)
Age at first epilepsy diagnosis, years, mean (SD)	2.2 (2.3)	11.1 (17.5)	5.6 (6.5)	4.2 (4.2)	7.9 (13.5)
Age at initial epilepsy diagnosis available, n	45	162	108	26	315 (76)
Age <18 years at initial epilepsy diagnosis, n (%)	45 (100)	131 (81)	99 (92)	25 (96)	275 (87)
At least one EEG, n (%)	47[b] (96)	165 (70)	104 (81)	28 (100)	316 (77)
With slow spike waves, n (%)	16[b] (34)	13 (10)	10[b](10)	1 (4)	39 (12)
Helmet supply, n (%)	17 (35)	4 (2)	30 (23)	28 (100)	51 (12)

[a]Calculation without Centre 2; [b]One missing documentation (indication 'n.a.') that was evaluated as 'no'.
EEG, electroencephalogram; LGS, Lennox-Gastaut syndrome; MZEB, medical centres for adults with disabilities; NA, not assessed; SD, standard deviation.

- Among patients with available age at diagnosis, 92% with potential LGS and 81% classed as LGS unlikely were diagnosed with epilepsy before 18 years of age, compared with 100% of those with an existing LGS diagnosis (**Table 2**)
- Patients with 'Potential LGS' were younger than those with no LGS documentation overall at time of first epilepsy diagnosis (mean age 5.6 vs 8.9 years)

Figure 2. Age distribution at first epilepsy diagnosis of patients identified as 'Potential LGS'



LGS, Lennox-Gastaut syndrome; NK, not known/missing documentation.

- The EpiDIAL algorithm did not include an age-of-onset criterion; a small proportion (~9%) of patients identified as 'Potential LGS' were first diagnosed with epilepsy at ≥15 years of age (**Figure 2**)

Table 3. Sensitivity analyses: identification of potential LGS

Criterion 2a	No LGS documentation (N=363)	LGS diagnosed (N=49)
Main analysis ≥2 seizure types, must include tonic seizures, n (%)	**128 (35)**	44 (90)
Sensitivity analysis 1: ≥2 seizure types (no obligation of tonic seizure), n (%)	132 (36)	44 (90)
Sensitivity analysis 2: ≥3 seizure types (no obligation of tonic seizure), n (%)	83 (23)	36 (73)

LGS, Lennox-Gastaut syndrome.

- The EpiDIAL algorithm identified 90% of diagnosed cases as having potential LGS (**Table 3**)
  - The five cases not identified all fulfilled Criterion 1 but not Criterion 2
- Removing the requirement for tonic seizures had only a minor effect on patient identification rates
- Requiring ≥3 seizure types[a] lowered the identification rates among the 'LGS diagnosed' and 'No LGS documentation' populations

[a]Tonic, axial-tonic, absence or atonic seizures.

Data availability and study limitations

- There was substantial heterogeneity in documentation practice, including coding of LGS characteristics, and data availability at the participating centres, with not all having digital charts available
  - Among 'No LGS documentation' files across the four centres, 75–88% met Criterion 1 and 14–61% met Criterion 2
  - The rate of 'Potential LGS' among these files ranged from 14–56% across the four centres, and of 'High-potential LGS' from 0–32%
- This study was based on retrospective data from four specialist centres for adults with disabilities and may not be representative of a wider population

Conclusions

- Using this simple, sensitive algorithm, approximately one-third (35%) of patients with epilepsy and intellectual disability met criteria for potential, yet undocumented, LGS
  - Lack of a diagnosis may hinder access to appropriate treatment, and thus seizure management may not be optimal in these patients
- Inclusion of an age-related criterion could be considered for a future iteration of the algorithm, while setting Criterion 1a as mandatory might better differentiate for patients with treatment-resistant epilepsy. Furthermore, it may also be of interest to compare the results observed here with the use of another validated algorithm, such as REST-LGS, in this cohort
- These findings provide valuable information on the potential prevalence of undiagnosed LGS in adults with intellectual disabilities, and the importance of patient re-evaluation in adulthood to improve screening and help ensure access to appropriate treatment options for patients

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