Poster #

Analysis of Physician Notes to Examine the Clinical and Humanistic Burden of Patients With Dravet Syndrome and Lennox-Gastaut Syndrome in the United States

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Introduction

- Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) are rare, childhood-onset, developmental epileptic encephalopathies that are distinguished by unpredictable and frequent seizures[1,2]
- Both diseases are associated with a wide range of developmental delays in most children, including learning disability, cognitive, and behavioral issues, profoundly impacting patients' and caregivers' lives[1,2]
- Standard of care typically includes antiseizure medications (ASMs) and expands to heterogeneous adjunct therapy, and even surgery in some cases, to attempt seizure control[1,3,4]
- However, despite recent advancements of clinical and nonclinical interventions, patients with DS and LGS continue to experience substantial burden in their intellectual development, social functioning, and quality of life (QOL)[3,5]
- There are limited data available quantifying clinical and humanistic burden of nonseizure symptoms and safety issues related to current ASM use in these patients

Objective

- To characterize the clinical and humanistic burden of DS and LGS, including seizure and nonseizure burden and patients' QOL

Methods

- This retrospective analysis included data from Amplity Insight's database of medical transcription records, capturing routine care in the United States (US) from January 2010 to January 2022
- The database of approximately 55 million medical transcription records included inpatient and outpatient electronic, unstructured, records from approximately 25 million patients and 150,000 multispecialty physicians
- Natural language processing (NLP) technology retrospectively analyzed physician–patient interactions recorded in the database
- Eligible patients had ≥ 1 inpatient or outpatient record and a diagnosis of DS or LGS, based on symptoms and/or genetic or electroencephalography findings, and mention of treatment with ≥ 1 ASM
- Descriptive patient-level characteristics, seizure and nonseizure burden, and QoL impacts were described

Results

Patient demographics

- NLP queries identified 166 patients with DS and 1063 patients with LGS who were treated with ≥ 1 ASM
- Demographics and patient characteristics are shown in **Table 1**
- Overall, among patients with recorded data at the time of the healthcare provider visit (DS: n = 121; LGS: n = 877):
  - Pediatric patients aged < 18 years were more prevalent in the DS group (83%) and adult patients aged ≥ 18 years were more prevalent in the LGS group (58%)
- Mean age at diagnosis for patients with recorded data (DS: n = 9; LGS: n = 53) was 1.1 years for patients with DS and 2.1 years for those with LGS
- Most patients with recorded data were White (DS: 95%; LGS: 90%)

Table 1. Demographics and Characteristics of Patients With DS or LGS

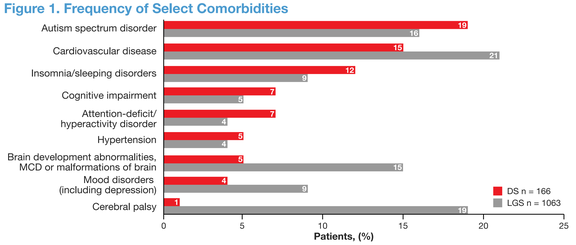
Characteristics	DS	LGS
Total patients, n	166	1063
Age at first visit[a], n	121	877
Mean (median) years	12 (9)	24 (20)
Pediatric (aged 0–17 years), n (%)	101 (83)	370 (42)
Adult (aged 18+ years), n (%)	20 (17)	507 (58)
Age at diagnosis, n	9	53
Mean (median) years	1.1 (0.3)	2.1 (0.9)
Age at diagnosis, min–max years	0.2–6.0	0.2–8.0
Sex, n	162	1050
Female, n (%)	76 (47)	397 (38)
Male, n (%)	86 (53)	653 (62)
Race or ethnicity, n	39	338
White, n (%)	37 (95)	303 (90)
African American or Black, n (%)	1 (3)	25 (7)
Hispanic, n (%)	1 (3)	10 (3)
Asian, n (%)	0 (0)	0 (0)
Other, n (%)	0 (0)	0 (0)
US Census region[b], n	164	1001
South, n (%)	75 (46)	436 (44)
Northeast, n (%)	56 (34)	256 (26)
West, n (%)	29 (18)	190 (19)
Midwest, n (%)	15 (9)	181 (18)
Top 3 specialties of healthcare providers, n	166	1063
Primary care, n (%)	71 (43)	349 (33)
Pediatrics, n (%)	47 (28)	140 (13)
Neurology or epileptology, n (%)	29 (17)	262 (25)
Antiseizure medications used[c], n	166	1063
Valproic acid/Divalproex, n (%)	95 (58)	423 (40)
Clobazam, n (%)	88 (54)	516 (49)
Levetiracetam, n (%)	87 (53)	496 (47)
Diazepam (oral and rectal), n (%)	67 (41)	311 (30)
Unspecified ASM, n (%)	2 (1)	14 (1)

[a]Oldest age given if age is reported on multiple records for a patient in study database. [b]Region where provider is located. [c]Percentages can add up to be more than 100% because patients could be using more than one type of ASM. Only the most commonly used ASMs are listed.
ASM, antiseizure medication; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; min, minimum; max, maximum; US, United States.

Comorbidities

- Half (50%) of the patients with DS mentioned comorbidities, with the 3 most commonly reported being autism spectrum disorder (19%), cardiovascular disease (CVD) (15%), and insomnia/sleeping disorders (12%) (**Figure 1**)
- Among patients with LGS, 63% reported comorbidities, with CVD (21%), cerebral palsy (19%), and autism spectrum disorder (16%) being the 3 most common (**Figure 1**)

Figure 1. Frequency of Select Comorbidities

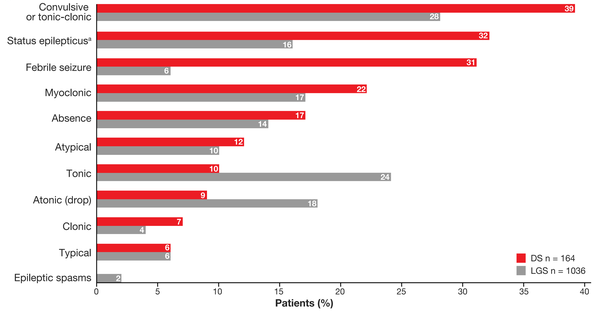


DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; MCD, malformations of cortical development.

Seizure characteristics

- A total of 164 (99%) patients with DS and 1036 (97%) patients with LGS reported seizures (**Figure 2**)
- Among the reported seizures in patients with DS or LGS, causes of onset were unknown in 48% and 55%; generalized in 38% and 38%; and focal in 15% and 7%, respectively
- The 3 most common types of seizures mentioned among patients with DS were: convulsive or tonic–clonic (39%), status epilepticus (32%; defined as a seizure or cluster seizure that lasts > 5 minutes), and febrile (31%)
- Among patients with LGS, the most common seizures were convulsive (28%), tonic (24%), and atonic (drop) (18%)
- A small subset of patients in each group (DS, 3% [n = 5]; LGS, 5% [n = 57]) reported seizure-related injuries, with 2% (n = 3) of patients with DS reporting superficial injuries (eg, burns) and 4% (n = 37) of patients with LGS reporting craniocerebral injury and brain injury
- Of the patients who mentioned the frequency of their seizures (DS: n = 18; LGS, n = 181), 83% with DS and 92% with LGS reported having seizures daily

Figure 2. Frequency of Common Seizure Types

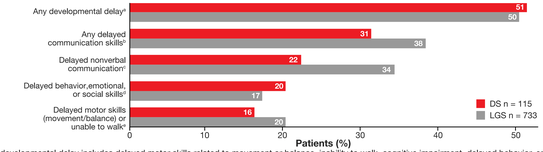


[a]Status epilepticus is defined as a seizure or cluster seizure series lasting > 5 minutes.
DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

Nonseizure symptoms

- Among patients with DS or LGS, 69% (DS: n = 115; LGS: n = 733) reported experiencing nonseizure symptoms (**Figure 3**)
- For both patients with DS or LGS, developmental and communication skills were the most frequently impacted
  - Half of all patients with DS (51%) and LGS (50%) experienced developmental delays, which primarily included delayed motor skills, delayed behavior, and growth and nutrition issues
    - Notably, for both indications, more pediatric patients experienced delayed motor skills impacting their movements, balance, and mobility compared with adult patients (DS: 19% vs 0%; LGS: 31% vs 7%, respectively)
    - Whereas issues related to growth and nutrition were observed in more adult patients with DS or LGS than in pediatric patients (DS: 30% vs 17%; LGS: 20% vs 12%, respectively)
  - Communication skills, including verbal and nonverbal skills, were delayed in 31% and 38% of all patients with DS or LGS, respectively
    - Issues with verbal communication were more common in pediatric patients versus adult patients in both diseases (DS: 16% vs 5%; LGS: 11% vs 3%, respectively)
    - More adult patients with DS had nonverbal communication deficits than pediatric patients (40% vs 18%, respectively); among those with LGS, a similar percentage (35%) of pediatric and adult patients had these deficits

Figure 3. Frequency of Nonseizure Symptoms

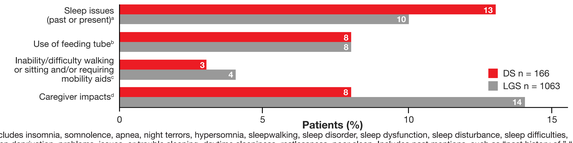


[a]Any developmental delay includes delayed motor skills related to movement or balance, inability to walk, cognitive impairment, delayed behavior, emotional, or social skills, learning disability, inability to focus, attention issues, memory issues, growth and nutrition issues, sensory integration disorders, dysautonomia, and sleep issues. [b]Delayed communication skills includes language, speech, and nonverbal expressions. [c]Delayed nonverbal communication includes eye contact and nonverbal expressions such as gestures and body language. [d]Excludes disruptive behavior. [e]Delayed motor skills related to movement or balance includes difficulty in motor skills while sitting or crawling, hypotonia, ataxia, delayed walking, and abnormal gait.
DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

Quality of life

- QOL impacts on patients included sleep issues (DS: 13%; LGS: 10%), feeding-tube use (DS: 8%; LGS: 8%), and inability or difficulty walking or sitting and/or requiring mobility aids (DS: 3%; LGS: 4%) (**Figure 4**)
- Caregivers' burden was mentioned in records for 8% of patients with DS and 14% of patients with LGS

Figure 4. Frequency of QOL Impacts



[a]Includes insomnia, somnolence, apnea, night terrors, hypersomnia, sleepwalking, sleep disorder, sleep dysfunction, sleep disturbance, sleep difficulties, sleep deprivation, problems, issues, or trouble sleeping, daytime sleepiness, restlessness, poor sleep. Includes past mentions, such as "past history of," "did suffer from," "no longer has" etc. [b]Eg, NG tube, X-tube, G-tube, J-tube, gastric tube, jejunum tube, gastronomy tube feeding, and feeding tube; [c]Includes terms regarding walking, sit/seating, moving, ambulation such as trouble, issue, inability, problem, difficulty etc. Mentions of mobility aid, scooter, wheelchair, cane, walking stick, stair-lift etc. [d]Caregiver, guardian, caretaker or mentions of person(s) helping the patient, be it a name (encrypted), family member, friend etc, eg, "sister is caring for the patient." Includes mention of lost work days, Family and Medical Leave Act, and disability.
ASM, antiseizure medication; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; QOL, quality of life.

Limitations

- The study includes limited data or potential underreporting for certain outcomes
- Lack of longitudinal follow-up of the transcription data source limits the full understanding of the patient journey and impact of medical conditions that may evolve or change beyond one or a few visits

Conclusions

- Analysis of this transcription database revealed that despite treatment with ASMs, patients with DS or LGS experience seizures, nonseizure symptoms, and QOL burdens that extend to caregivers
- Application of NLP to future research merits further consideration

Disclosures

ML and **SR** are employees of Takeda Pharmaceuticals USA, Inc., and are Takeda shareholders. **DI, PR,** and **FO** are employees of Amplity Health. **SWW** is a partner in Wade Outcomes Research and Consulting, and a consultant to Amplity Health.

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