**Supplementary material**

**Appendix Table S1**ATC/ICD-10 codes used in the patient selection algorithm.

|  |  |  |  |
| --- | --- | --- | --- |
| Classification code | Category | Description | Diagnosis code |
| ICD-10 | Epilepsy | Epilepsy and recurrent seizures | G40/G41 |
| Inclusionary developmental delay diagnoses | Developmental reading disorder, unspecified | F81.0 |
| Alexia | R48.0 |
| Developmental dyslexia | F81.0 |
| Other specific developmental reading disorder | F81.1 |
| Mathematics disorder | F81.2 |
| Other specific developmental learning difficulties | F81.8 |
| Expressive language disorder | F80.1 |
| Mixed receptive-expressive language disorder | F80.2 |
| Speech and language developmental delay due to hearing loss | F80.8 |
| Childhood onset fluency disorder | F80.8 |
| Other developmental speech or language disorder | F80.8, F80.9 |
| Developmental coordination disorder | F82 |
| Mixed development disorder | F82 |
| Other specified delays in development | F88 |
| Unspecified delay in development | F81.9, F89 |
| Mild intellectual disabilities | F70 |
| Moderate intellectual disabilities | F71 |
| Severe intellectual disabilities | F72 |
| Profound intellectual disabilities | F73 |
| Unspecified intellectual disabilities | F79 |
| Cerebral degeneration of childhood in other diseases classified elsewhere | G93.9 |
| Exclusionary competing etiologies | Malignant neoplasm of cerebrum, except lobes and ventricles | C71.0 |
| Malignant neoplasm of frontal lobe | C71.1 |
| Malignant neoplasm of temporal lobe | C71.2 |
| Malignant neoplasm of parietal lobe | C71.3 |
| Malignant neoplasm of occipital lobe | C71.4 |
| Malignant neoplasm of ventricles | C71.5 |
| Malignant neoplasm of cerebellum nos | C71.6 |
| Malignant neoplasm of brain stem | C71.7 |
| Malignant neoplasm of other parts of the brain | C71.8 |
| Malignant neoplasm of brain, unspecified | C71.9 |
| Alzheimer’s disease | G30.9+ |
| Pick disease | G31.0 |
| Other frontotemporal dementia | G31.0 |
| Senile degeneration of brain | G31.1 |
| Communicating hydrocephalus | G91.0 |
| Obstructive hydrocephalus | G91.1 |
| Idiopathic normal pressure hydrocephalus | G91.20 |
| Corticobasal degeneration | G31.0 |
| Cerebral degeneration, unspecified | G94 |
|  | Reye syndrome | G93.7 |
| Dementia with Lewy bodies | G31.82 |
| Other cerebral degeneration | G31.88 |
| Cerebral degeneration, unspecified | G31.9 |
| Paralysis agitans | G20 |
| Secondary parkinsonism | G21 |
| Other degenerative diseases of the basal ganglia | G23 |
| Essential and other specified forms of tremor | G25.0, G25.1, G25.2 |
| Tics of organic origin | G25.6 |
| Huntington’s chorea | G10 |
| Other choreas | G25.4, G25.5 |
| Stiff-man syndrome | G25.88 |
| Neuroleptic malignant syndrome | G21.0 |
| Benign shuddering attacks | G25.3 |
| Restless legs syndrome | G25.81 |
| Other extrapyramidal disease and abnormal movement disorders | G25.88, G25.9 |
| Friedreich ataxia | G11.1 |
| Hereditary spastic paraplegia | G11.4 |
| Primary cerebellar degeneration | G11.0, G11.1, G11.2 |
| Other cerebellar ataxia | G11.1 |
| Cerebellar ataxia in disease classified elsewhere | G32.8 |
| Other spinocerebellar disease | G11.3, G11.8 |
| Spinocerebellar disease, unspecified | G11.9 |
| Werdnig-Hoffmann disease | G12.0 |
| Spinal muscular atrophy, unspecified | G12.9 |
| Kugelberg-Welander disease | G12.1 |
| Other spinal muscular atrophy | G12.8 |
| Amyotrophic lateral sclerosis | G12.2 |
| Progressive muscular atrophy | G12.2 |
| Progressive bulbar palsy | G12.2 |
| Pseudobulbar palsy | G12.8 |
| Other motor neuron disease | G12.2 |
| Multiple sclerosis | G35 |
| Down syndrome | Q90 |
| Tuberous sclerosis | Q85.1 |
| Congenital hydrocephalus | Q03 |
| Other specified congenital anomalies of the brain | Q04 |
| Unspecified congenital anomaly of brain, spinal cord, and nervous system | Q07.9 |
| Abnormal brain development | Cerebral palsy | G80 |
| Hydrocephalus | G91 |
| Cerebral cysts | G93.0 |
| Anoxic brain damage, not elsewhere classified | G93.1 |
| ATC | Medication | Antiepileptic drugs | N03A |
| Rufinamide | N03AF03 |
| Felbamate | N03AX10 |
| Dibro-Be-mono 850 mg (PZN: 4648235) | N03AX31 |
| Stiripentol | N03AX17 |
| Valproate | N03AG01 |
| Clobazam | N05BA09 |
| Carbamazepine | N03AF01 |
| Oxcarbazepine | N03AF02 |
| Eslicarbazepine | N03AF04 |
| Phenytoin | N03AB02 |
| Lacosamide | N03AX18 |
| Lamotrigine | N03AX09 |

ATC, Anatomical Therapeutic Chemical Classification System; ICD-10, International Classification of Diseases, 10th Revision.

**Appendix Table S2**Summary of published healthcare insurance data in probable LGS.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author | Database(s) used | Data review period | No. of patients | Mean annual cost, per patient per year | Biggest cost contributors |
| Strzelczyk et al 2020 | Vilua Healthcare, Germany | January 1, 2007 to December 31, 2016 | Probable LGS with epilepsy diagnosis before 6 years of age: 208 | All patients: €22,787  With prescribed rescue medication: €33,872  Without prescribed rescue medication: €13,785 | Inpatient care  Home nursing care  Medication |
| Reaven et al 2019 | Commercial and Medicaid insurance claims (Truven Health Analytics), USA | October 2010 to September 2015 | Commercial: 2269 patients with ‘possible’ LGS  Medicaid: 3730 with ‘possible’ LGS | Commercial: $65,937 (SD $96,223)  Medicaid: $64,885 (SD $86,000) | Commercial: Inpatient care  Medicaid: Home health services |
| Reaven et al 2018 | Commercial and Medicaid insurance claims (Truven Health Analytics), USA | October 2010 to September 2015 | Commercial: 2270 patients with ‘possible’ LGS  Medicaid: 3749 patients with ‘possible’ LGS | Commercial: $65,026 (SD $34,324)  Medicaid: $63,930 (SD $45,761) | Commercial: Inpatient care  Medicaid: Home health services |
| Piña-Garza et al 2017 | Medicaid  multi-state database, USA | Florida: Q3 1997–Q2 2012 Iowa: Q1 1998–Q1 2013 Kansas: Q1 2001–Q1 2013 Mississippi: Q1 2006–Q4 2013  Missouri: Q1 1997–Q1 2013 New Jersey: Q1 1997–Q1 2013 | Probable LGS: 14,712  Non-LGS: 353,281 | Probable LGS: $28,461–$40,193  Non-LGS:  $7,170–$25,901 | Probable LGS: Medical costs |
| François et al 2017 | The MarketScan®, Commercial, Medicare Supplemental, and Medicaid databases, USA | October 1, 2010 to March 31, 2014 | MarketScan and Medicare: 1974 patients with LGS; 590 received clobazam  Medicaid: 2012 patients with LGS; 647 received clobazam | MarketScan and Medicare  Clobazam: $73,486 (SD $110,918)  Non-clobazam: $49,632 (SD $89,843)  Medicaid  Clobazam: $62,989 (SD $120,325)  Non-clobazam: $38,370 (SD $70,243) | MarketScan and Medicare  Clobazam: Hospitalization  Non-clobazam: Hospitalization  Medicaid  Clobazam: Other outpatient  Non-clobazam: Other outpatient |

LGS, Lennox-Gastaut syndrome; Q, quarter; SD, standard deviation.