**Epidemiology, Healthcare Resource Use, and Mortality in Patients With Probable Dravet Syndrome: A Population-Based Study on German Health Insurance Data**

**Supplementary Material**

**Supplementary Table 1**ATC/ICD-10 codes used in the patient selection algorithm.

|  |  |  |  |
| --- | --- | --- | --- |
| **Code** | **Category** | **Description** | **Code** |
| **ICD-10** | TSC | Tuberous sclerosis | Q85.1 |
| 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’s 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 (INPH) | G91.20 |
| Corticobasal degeneration | G31.0 |
| Cerebral degeneration, unspecified | G94 |
| Reye’s 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 (RLS) | G25.81 |
| Other extrapyramidal disease and abnormal movement disorders | G25.88, G25.9 |
| Friedrich’s 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 | Antiepileptics (AEDs) | 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;
TSC, tuberous sclerosis complex.

**Supplementary Table 2**

Annual total healthcare costs by age group for patients with probable DS during the 10-year study period.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **All patients** | **Years where patients prescribed with rescue medicationa** | **Years where patients not prescribed with rescue medicationa** | **P-valueb** |
| *Mean (SD) annual cost per age group per patient-year, €* |  |
| 0–1 year |  |  |  |  |
| Number of patients, n | 13 | 4 | 13 |  |
| Patient-years, n (%) | 24 | 4 (17) | 20 (83) |  |
| Cost, €  | 6,520 (17,600) | 21,802 (39,363) | 3,463 (8,446) | 0.078 |
| 2–9 years |  |  |  |  |
| Number of patients, n | 28 | 24 | 25 |  |
| Patient-years, n (%) | 141 | 63 (45) | 78 (55) |  |
| Cost, €  | 14,285 (29,933) | 16,736 (27,932) | 12,305 (31,496) | 0.061 |
| 10–19 years |  |  |  |  |
| Number of patients, n | 33 | 15 | 28 |  |
| Patient-years, n (%) | 137 | 35 (26) | 102 (74) |  |
| Cost, €  | 13,778 (21,673) | 13,477 (16,679) | 13,881 (23,213) | 0.763 |
| 20–29 years |  |  |  |  |
| Number of patients, n | 43 | 15 | 43 |  |
| Patient-years, n (%) | 216 | 35 (16) | 181 (84) |  |
| Cost, €  | 9,556 (19,737) | 16,533 (25,033) | 8,206 (18,320) | 0.004 |
| 30–39 years |  |  |  |  |
| Number of patients, n | 40 | 5 | 40 |  |
| Patient-years, n (%) | 187 | 12 (6) | 175 (94) |  |
| Cost, €  | 7,248 (12,189) | 22,449 (20,246) | 6,206 (10,765) | < 0.001 |
| 40–49 years |  |  |  |  |
| Number of patients, n | 46 | 8 | 44 |  |
| Patient-years, n (%) | 204 | 28 (14) | 176 (86) |  |
| Cost, €  | 10,053 (15,097) | 15,972 (15,486) | 9,111 (14,862) | 0.001 |
| 50–59 years |  |  |  |  |
| Number of patients, n | 42 | 5 | 41 |  |
| Patient-years, n (%) | 203 | 8 (4) | 195 (96) |  |
| Cost, €  | 10,731 (18,882) | 16,818 (25,479) | 10,481 (18,607) | 0.509 |
| 60–69 years |  |  |  |  |
| Number of patients, n | 23 | 2 | 23 |  |
| Patient-years, n (%) | 95 | 7 (7) | 88 (93) |  |
| Cost, € | 13,558 (25,262) | 8,624 (9,691) | 13,951 (26,095) | 0.019 |
| 70–79 years |  |  |  |  |
| Number of patients, n | 8 | 1 | 8 |  |
| Patient-years, n (%) | 39 | 2 (5) | 37 (95) |  |
| Cost, €  | 21,988 (43,039) | 12,197 (17,249) | 22,517 (44,062) | 0.092 |
| 80+ yearsNumber of patients, nPatient-years, n (%)Cost, € | 3155,296 (11,515) | ––– | 315 (100)5,296 (11,515) | NA |

DS, Dravet syndrome; NA, not applicable; SD, standard deviation.

a Rescue medication prescription is defined by having at least 1 prescription of midazolam, diazepam (rectal formulation), or chloral hydrate. b T-test for patients with rescue medication prescription vs. patients without rescue medication prescription.