Epilepsy/Antiepileptic drug response algorithm

\*Part 2 of the algorithm is NOT for network implementation

**Background**

70% of patients with new-onset epilepsy respond to Antiepileptic (AED) treatment (goal seizure freedom):

 ~40% to the first AED

 ~30% to the second AED

~30% to the third and fourth AED

~30% never respond: Drug-resistant epileptics

Identification of drug-resistant patients allows other treatment options:

 Epilepsy surgery

 Vagus nerve stimulator (VNS)

 Ketogenic or modified Atkins diets

Definitions of drug-resistant and drug-responder according to ILAE (*Epilepsia. 2010;51(6):1069-77*)

* **Drug-resistant epilepsy**: Failure of adequate trials of two tolerated, appropriately chosen and used AED schedules (monotherapy or combination) to achieve sustained seizure freedom
* **Drug response**: Seizure freedom >= 1 year or at least three times the longest inter-seizure interval

**Part 1: Identification of epilepsy subjects and controls:**

* **Case inclusion criteria:**

-Two or more relevant ICD-9 or ICD10 codes for epilepsy (Table 1) in two or more in-person visits

*AND*

-One or more prescription of AEDs (Table 2)

OR

-Three or more relevant relevant ICD-9 or ICD10 codes for epilepsy (Table 1) in three or more in-person visits.

* **Case exclusion criteria:**

**-**Any ICD9-ICD10 codes shown in Table 3

* **Controls:**

-No diagnosis codes for epilepsy (Table 1)

-No history of relevant medications (Table 2)

-No diagnosis codes shown in Table 3

-Must have two or more in person visits in the last 5 years

 **Covariates**

* Age at diagnosis
* Gender
* Ethnicity
* Epilepsy subtype
* Specific AEDs tried
* Visits follow up

**PART 2 IS NOT FOR NETWORK IMPLEMENTATION**

**Part 2: Definition of drug resistant epilepsy**

**Drug-resistant epileptic** is defined as any subject meeting at least one of the following criteria:

≥5 different AEDs listed in the EMR

*OR*

≥3 AEDs ineffective

*OR*

History of ketogenic diet

*OR*

History of epileptic surgery or VNS

**Drug responder epileptic** is defined as any subject meeting at least one of the following criteria:

Seizure freedom ≥ 365 days

*OR*

AED wean-off due to seizure freedom

*OR*

<3 AEDs prescribed *AND* time on same AED ≥ 365 days (monotherapy or in combination)

**Variables:**

* Number of ineffective AEDs\*
* Period of seizure freedom\*
* Record of AED wean-off\*

\* The brief clinical history included in the EEG was used to capture these data but also a NLP search on the clinical letters was performed for completeness

 **Table 1- Inclusionary codes**

|  |  |
| --- | --- |
| **ICD9** | **Diagnosis name** |
| 345.0 | Generalized nonconvulsive epilepsy |
| 345.1 | Generalized convulsive epilepsy |
| 345.2 | Petit mal status |
| 345.3 | Grand mal status |
| 345.4 | Localization-related (focal) (partial) epilepsy and epileptic syndromes with complex partial seizures |
| 345.5 | Localization-related (focal) (partial) epilepsy and epileptic syndromes with simple partial seizures |
| 345.6 | Infantile spasms |
| 345.7 | Epilepsia partialis continua |
| 345.8 | Other forms of epilepsy and recurrent seizures |
| 345.9 | Epilepsy, unspecified |
| **ICD10** | **Diagnosis name** |
| G40.0 | Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset |
| G40.1 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures |
| G40.2 | Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures |
| G40.3 | Generalized idiopathic epilepsy and epileptic syndromes |
| G40.A | Absence epileptic syndrome |
| G40.B | Juvenile myoclonic epilepsy [impulsive petit mal] |
| G40.4 | Other generalized epilepsy and epileptic syndromes |
| G40.5 | Epileptic seizures related to external causes |
| G40.8 | Other epilepsy and recurrent seizures |
| G40.9 | Epilepsy, unspecified |

**Table 2-Relevant medications**

|  |
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| **Antiepileptic Medication** |
| **Generic name** | **Brand name** |
| Valproic acid/Sodium valproate  | Divalproex®, Depakote®, Depakene® |
| Phenytoin  | Dilantin® |
| Carbamazepine  | Tegretol®, Tegretol® XR, Carbatrol® |
| Oxcarbazepine  | Trileptal® |
| Lamotrigine  | Lamictal® |
| Levetiracetam  | Keppra® |
| Ethosuximide  | Zarontin® |
| Topiramate  | Topamax® |
| Zonisamide  | Zonegran® |
| Lacosamide  | Vimpat® |
| Rufinamide  | Banzel® |
| Gabapentin  | Neurontin® |
| Vigabatrin  | Sabril® |
| Tiagabin  | Gabitril® |

**Table 3 - Exclusionary codes**

|  |  |
| --- | --- |
| **ICD-9 code** | **Diagnosis name** |
| 191.x | Malignant neoplasms of brain |
| 198.x | Secondary malignant neoplasm of other specified sites |
| 225.x | Benign neoplasm of brain and other parts of nervous system |
| 228.02 | Hemangioma of intracranial structures |
| 237.5 | Brain and spinal cord |
| 237.6 | Meninges |
| 237.9 | Other and unspecified parts of nervous system |
| 239.6 | Neoplasms of unspecified nature of the brain |
| 270.x | Disorders of amino-acid transport and metabolism |
| 271.0 | Glycogenosis |
| 271.8 | Glucose Transporter Type 1 Deficiency Syndrome |
| 277.5 | Mucopolysaccharidosis |
| 277.86 | Peroxisomal disorders |
| 277.87 | Mitochondrial metabolism disorders |
| 334.2 | Primary cerebellar degeneration |
| 359.9 | Spinocerebellar disease, unspecified |
| 318.1 | Severe mental retardation |
| 318.2 | Profound mental retardation |
| 323.9 | Unspecified causes of encephalitis |
| 54.3 | Herpetic meningoencephalitis |
| 330.x | Cerebral degenerations usually manifest in childhood |
| 331.x | Other cerebral degenaration |
| 340 | Multiple sclerosis |
| 341.x | Other demyelinating diseases of central nervous system |
| 430.x-438.x | Cerebrovascular disease |
| 740.x | Anencephalus and similar anomalies |
| 741.x | Spina bifida |
| 742.x | Other congenital anomalies of nervous system |
| 758.x | Chromosomal anomalies |
| 759.8 | Other specified anomalies |
| 759.81 | Prader-Willi syndrome |
| 759.83 | Fragile X syndrome |
| 852.x-854.x | Intracranial Injury |
| V10.85 | Personal history of malignant neoplasm of the brain |
| V12.41 | Benign neoplasm of the brain |
| V12.54 | Transient ischemic attack and cerebral infarction without residual deficits |
| **ICD10** | **Diagnosis name** |
| B00.4 | Herpesviral encephalitis |
| C71.x | Malignant neoplasm of the brain |
| C79.89 | Secondary malignant neoplasm of other specified sites |
| D33.x | Benign neoplasm of brain and other parts of nervous system |
| D18 | Hemangioma of intracranial structures |
| D42.x | Neoplasm of uncertain behavior of meninges |
| D43.x | Neoplasm of uncertain behavior of brain and central nervous system |
| D49.6 | Neoplasm of unspecified behavior of brain |
| E70.x | Disorders of aromatic amino-acid metabolism |
| E71.5 | Peroxisomal disorders |
| E72.x | Other disorders of amino-acid metabolism |
| E74.x | Other disorders of carbohydrate metabolism |
| E76.x | Disorders of glycosaminoglycan metabolism |
| E88.4 | Mitochondrial metabolism disorders |
| F72 | Severe intellectual disabilities |
| F73 | Profound intellectual disabilities |
| F84.2 | Rett's syndrome |
| G04.9 | Encephalitis, myelitis and encephalomyelitis, unspecified |
| G30.x | Alzheimer's disease |
| G31.x | Other degenerative diseases of nervous system, not elsewhere classified |
| G35 | Multiple sclerosis |
| G36.0 | Neuromyelitis optica [Devic] |
| G37.x | Other demyelinating diseases of central nervous system |
| G45 | Transient cerebral ischemic attacks and related syndromes |
| G72.9 | Myopathy |
| G91.x | Hydrocephalus |
| G94.x | Other disorders of brain in diseases classified elsewhere |
| I60.x | Nontraumatic subarachnoid hemorrhage |
|  I61.x | Nontraumatic intracerebral hemorrhage |
| I62.x | Other and unspecified nontraumatic intracranial hemorrhage |
| I63.x |  Cerebral infarction |
| I65.x | Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction |
| I66.x | Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction |
| I67.x | Other cerebrovascular diseases |
| I69.x | Sequelae of cerebrovascular disease |
| Q00.x – Q07.x | Other congenital malformations of the nervous system |
| Q87.1 | Congenital malformation syndromes predominantly associated with short stature |
| Q90-Q99 | Chromosomal abnormalities |
| S06.1 | Traumatic cerebral edema |
| S06.2 | Diffuse traumatic brain injury |
| S06.3 | Focal traumatic brain injury |
| S06.4 | Epidural hemorrhage |
| S06.5 | Traumatic subdural hemorrhage |
| S06.6 | Traumatic subarachnoid hemorrhage |
| S06.8 | Other specified intracranial injuries |
| S06.9 | Unspecified intracranial injury |
| Z85.841 | Personal history of malignant neoplasm of brain |
| Z86.011 | Personal history of benign neoplasm of the brain |
| Z86.73 | Personal history of transient ischemic attack (TIA), and cerebral infarction without residual deficits |

**Table 4 – Procedure codes**

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| **CPT Code** | **Description** |
| 61531 | Subdural implantation of strip electrodes through one or more burr or trephine hole(s) for long term seizure monitoring |
| 61533 | Craniotomy with elevation of bone flap; for implantation of an electrode array, for long term seizure monitoring |
| 61534 | Craniotomy with elevation of bone flap; for excision of epileptogenic focus without electrocorticography during surgery |
| 61535 | Craniotomy with elevation of bone flap; for removal of epidural or subdural electrode array, without excision of cerebral tissue (separate procedure) |
| 61536 | Craniotomy with elevation of bone flap; for excision of cerebral epileptogenic focus, with electrocorticography during surgery (includes removal of electrode array) |
| 61537 | Craniotomy with elevation of bone flap; for lobectomy, temporal lobe, without electrocorticography during surgery |
| 61538 | Craniotomy with elevation of bone flap; for lobectomy, temporal lobe, with electrocorticography during surgery |
| 61539 | Craniotomy with elevation of bone flap; for lobectomy, other than temporal lobe, partial or total, with electrocorticography during surgery |
| 61540 | Craniotomy with elevation of bone flap; for lobectomy, other than temporal lobe, partial or total, without electrocorticography during surgery |
| 61541 | Craniotomy with elevation of bone flap; for transection of corpus callosum |
| 61542 | Craniotomy with elevation of bone flap; for total hemispherectomy |
| 61543 | Craniotomy with elevation of bone flap; for partial or subtotal (functional) hemispherectomy |
| 61760 | Stereotactic implantation of depth electrodes into the cerebrum for long term seizure monitoring |
| 61885 | Incision and subcutaneous placement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array |
| 61888 | Revision or removal of cranial neurostimulator pulse generator or receiver |
| 64573 | Incision for implantation of neurostimulator electrodes; cranial nerve |
| 64585 | Revision or removal of peripheral neurostimulator electrodes |
| 95970 | Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex neurostimulator pulse generator, without reprogramming |
| 95974 | Complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, with or without nerve interface testing, first hour |
| 95975 | Complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, each additional 30 minutes after first hour (list separately in addition to code for primary procedure) ***(Use 95975 in conjunction with code 95974.)*** |