ICARE

Interagency Collaborative to Advance Research in Epilepsy

NIH Campus, Bethesda, MD

April 14, 2016

Ontologies: Applications to Epilepsy

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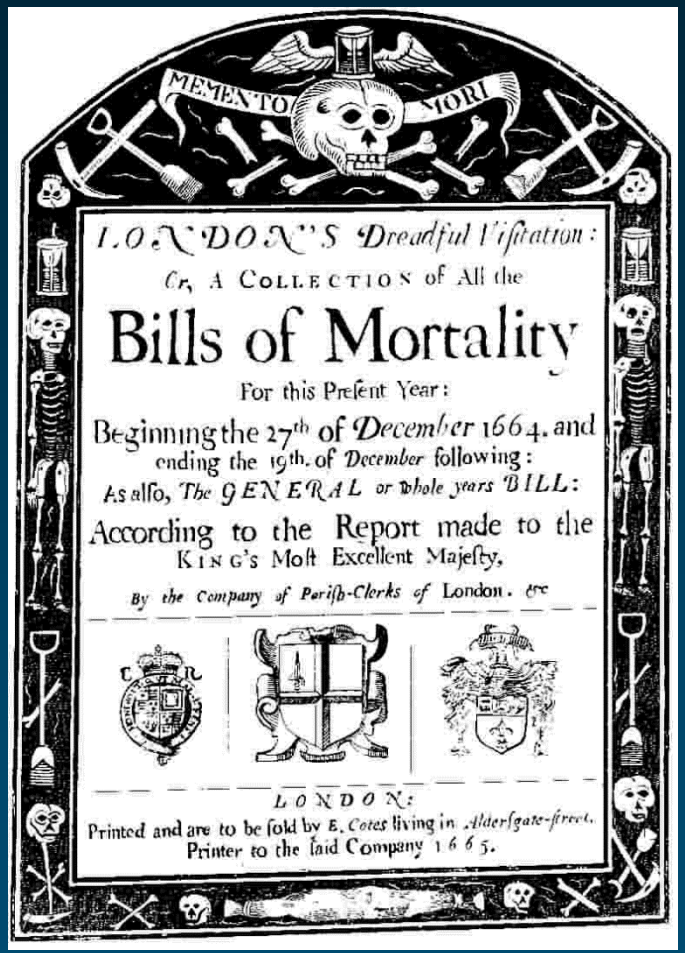
U.S. National Library of Medicine

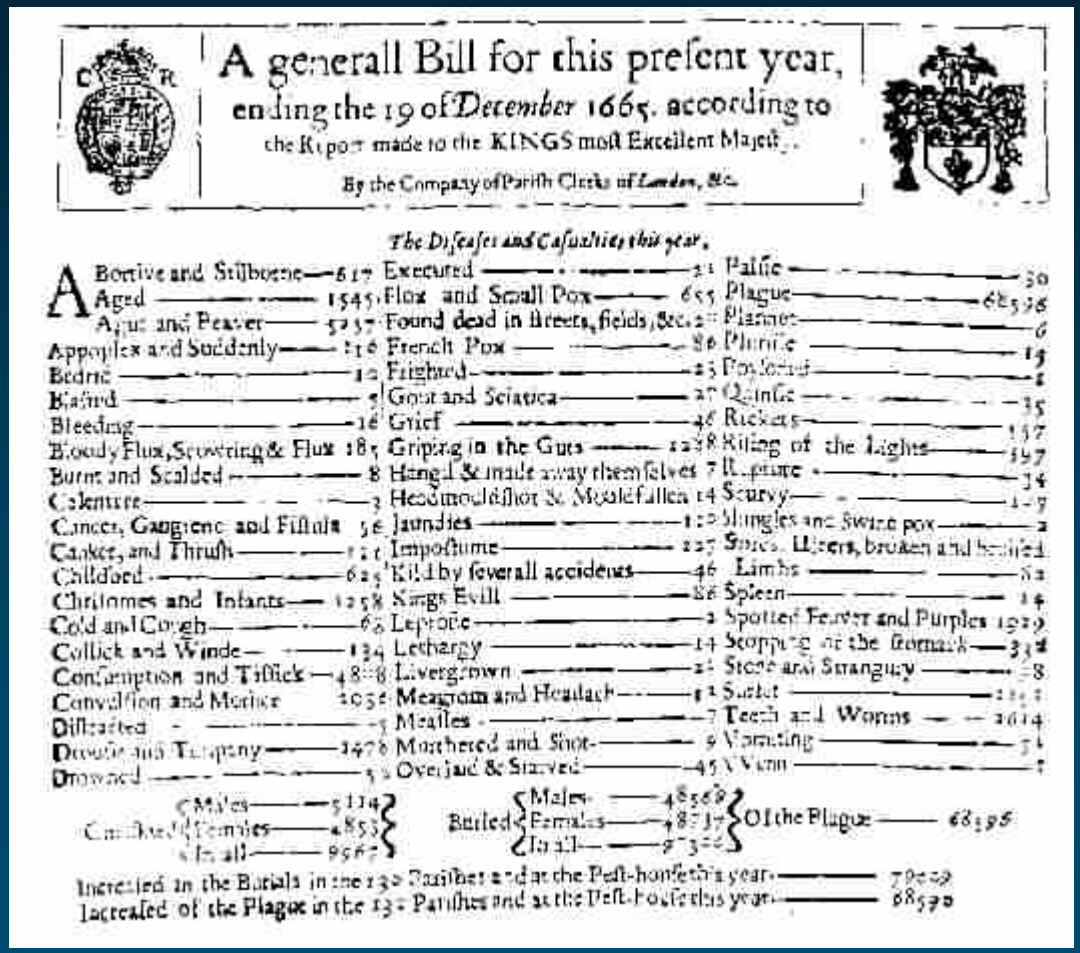
Outline

- Why do we need ontologies?
- Epilepsy in standard clinical ontologies
  - ICD-10
  - SNOMED CT
  - LOINC
  - RxNorm
- Beyond standard ontologies

Why do we need ontologies?

London Bills of Mortality





A generall Bill for this present year, ending the 19 of December 1665. according to the Report made to the KINGS most Excellent Majesty.

By the Company of Parish Clerks of London, &c.

The Diseases and Casualties this year.

Abortive and Stillborne	617	Executed	21	Palsie	50
Aged	1545	Flox and Small Pox	655	Plague	68596
Ague and Feaver	5257	Found dead in Streets, fields, &c.	2	Planet	6
Appoplex and Suddenly	116	French Pox	86	Pleurisie	15
Bedrid	12	Frighted	23	Poysoned	5
Blasted	5	Gout and Sciatica	20	Quinsie	35
Bleeding	16	Grief	46	Rickets	557
Bloody Flux, Scowring & Flux	185	Griping in the Guts	1288	Rising of the Lights	597
Burnt and Scalded	8	Hang'd & made away themselves	7	Rupture	34
Calenture	3	Headmould-shot & Mould-fallen	14	Scurvy	17
Cancer, Gangrene and Fistula	56	Jaundies	100	Shingles and Swine pox	2
Canker, and Thrush	211	Impostume	227	Sores, Ulcers, broken and bruised	
Childbed	625	Kill'd by severall accidents	46	Limbs	82
Chrisomes and Infants	1258	Kings Evill	86	Spleen	14
Cold and Cough	63	Leprosie	2	Spotted Feaver and Purples	1929
Collick and Winde	134	Lethargy	14	Stopping of the Stomach	334
Consumption and Tissick	4808	Livergrown	21	Stone and Strangury	98
Convulsion and Mother	1036	Meagrom and Headach	12	Suddat	2
Distracted	5	Measles	7	Teeth and Worms	2614
Dropsie and Tympany	1478	Murthered and Shot	9	Vomiting	54
Drowned	53	Overlaid & Starved	45	Worm	7

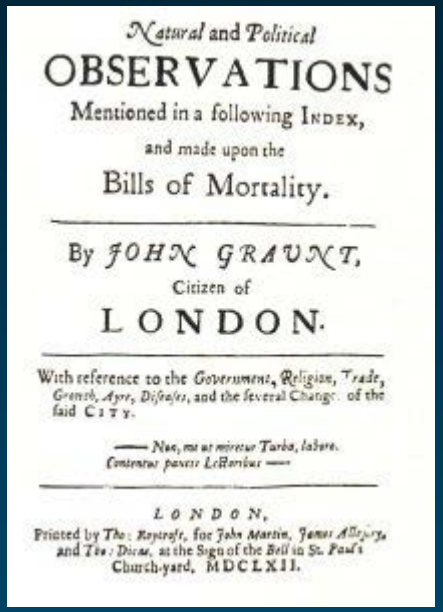
Christned: Males 5114, Females 4853, In all 9967.

Buried: Males 48568, Females 48137, In all 97305. Of the Plague 68596.

Increased in the Burials in the 130 Parishes and at the Pest-house this year 79025.
Increased of the Plague in the 130 Parishes and at the Pest-house this year 68590.

To support epidemiology

- John Graunt (1620-1674)
  - Analyzes the vital statistics of the citizens of London
- William Farr (1807-1883)
  - Medical statistician
  - Improves Cullen's classification
  - Contributes to creating ICD
- Jacques Berthillon (1851-1922)
  - Chief of the statistical services (Paris)
  - Classification of causes of death (161 rubrics)



Natural and *Political*

OBSERVATIONS

Mentioned in a following INDEX,

and made upon the

Bills of Mortality.

By JOHN GRAUNT,

Citizen of

LONDON.

With reference to the *Government*, *Religion*, *Trade*, *Growth*, *Ayre*, *Diseases*, and the several Changes of the said CITY.

Nec, me ut miretur Turba, laboro.
Contentus paucis Lectoribus.

LONDON,

Printed by *Tho: Roycroft*, for *John Martin*, *James Allestry*, and *Tho: Dicas*, at the Sign of the *Bell* in St. *Paul's* Church-yard, MDCLXII.

Limitations of existing classifications

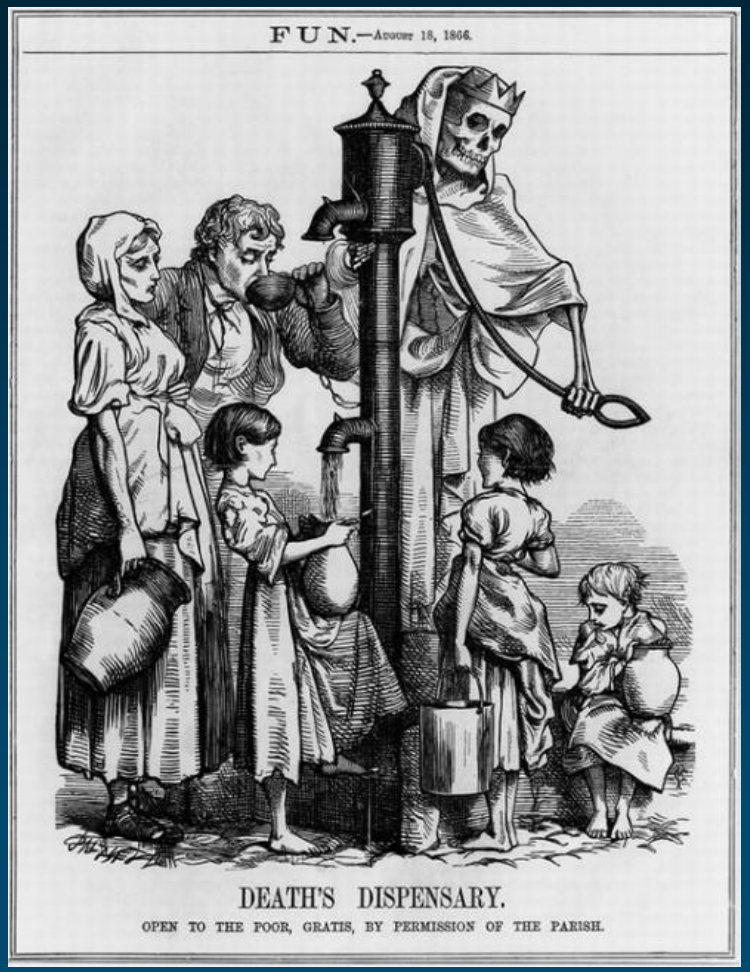
"The advantages of a uniform statistical nomenclature, however imperfect, are so obvious, that it is surprising no attention has been paid to its enforcement in Bills of Mortality. Each disease has, in many instances, been denoted by three or four terms, and each term has been applied to as many different diseases: vague, inconvenient names have been employed, or complications have been registered instead of primary diseases. The nomenclature is of as much importance in this department of inquiry as weights and measures in the physical sciences, and should be settled without delay."

– William Farr

First annual report.

London, Registrar General of England and Wales, 1839, p. 99.

From “bad air” to “bad water” (John Snow)



Epilepsy in standard clinical ontologies

http://apps.who.int/classifications/icd10/browse/

Internal Classification of Diseases

- ICD-10 Version:2016
  - I Certain infectious and parasitic diseases
  - II Neoplasms
  - III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
  - IV Endocrine, nutritional and metabolic diseases
  - V Mental and behavioural disorders
  - VI Diseases of the nervous system
    - G00-G09 Inflammatory diseases of the central nervous system
    - G10-G14 Systemic atrophies primarily affecting the central nervous system
    - G20-G26 Extrapyramidal and movement disorders
    - G30-G32 Other degenerative diseases of the nervous system
    - G35-G37 Demyelinating diseases of the central nervous system
    - G40-G47 Episodic and paroxysmal disorders
      - G40 Epilepsy
      - G41 Status epilepticus
      - G43 Migraine
      - G44 Other headache syndromes
      - G45 Transient cerebral ischaemic attacks and related syndromes
      - G46 Vascular syndromes of brain in cerebrovascular diseases
      - G47 Sleep disorders
    - G50-G59 Nerve, nerve root and plexus disorders
    - G60-G64 Polyneuropathies and other disorders of the peripheral nervous system
    - G70-G73 Diseases of myoneural junction and muscle
    - G80-G83 Cerebral palsy and other paralytic syndromes
    - G90-G99 Other disorders of the nervous system
  - VII Diseases of the eye and adnexa
  - VIII Diseases of the ear and mastoid process
  - IX Diseases of the circulatory system

Revision (ICD-10)-WHO Version for ;2016

Chapter VI
Diseases of the nervous system
(G00-G99)

Episodic and paroxysmal disorders
(G40-G47)

G40 Epilepsy

Excl.: Landau-Kleffner syndrome (F80.3)
seizure (convulsive) NOS (R56.8)
status epilepticus (G41.-)
Todd paralysis (G83.8)

G40.0 Localization-related (focal)(partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset
Benign childhood epilepsy with centrotemporal EEG spikes
Childhood epilepsy with occipital EEG paroxysms

G40.1 Localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures
Attacks without alteration of consciousness
Simple partial seizures developing into secondarily generalized seizures

G40.2 Localization-related (focal)(partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures
Attacks with alteration of consciousness, often with automatisms
Complex partial seizures developing into secondarily generalized seizures

G40.3 Generalized idiopathic epilepsy and epileptic syndromes
Benign:
- myoclonic epilepsy in infancy
- neonatal convulsions (familial)

Childhood absence epilepsy [pyknolepsy]
Epilepsy with grand mal seizures on awakening
Juvenile:
- absence epilepsy
- myoclonic epilepsy [impulsive petit mal]

Nonspecific epileptic seizures:
- atonic
- clonic
- myoclonic
- tonic
- tonic-clonic

NLM

http://apps.who.int/classifications/icd10/browse/

Internal Classification of Diseases

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  - VII Diseases of the eye and adnexa
  - VIII Diseases of the ear and mastoid process
  - IX Diseases of the circulatory system

G40.4 **Other generalized epilepsy and epileptic syndromes**

Epilepsy with:
- myoclonic absences
- myoclonic-astatic seizures

Infantile spasms

Lennox-Gastaut syndrome

Salaam attacks

Symptomatic early myoclonic encephalopathy

West syndrome

G40.5 **Special epileptic syndromes**

Epilepsia partialis continua [Kozhevnikof]

Epileptic seizures related to:
- alcohol
- drugs
- hormonal changes
- sleep deprivation
- stress

Use additional external cause code (Chapter XX), if desired, to identify drug, if drug-induced.

G40.6 **Grand mal seizures, unspecified (with or without petit mal)**

G40.7 **Petit mal, unspecified, without grand mal seizures**

G40.8 **Other epilepsy**

Epilepsies and epileptic syndromes undetermined as to whether they are focal or generalized

G40.9 **Epilepsy, unspecified**

Epileptic:
- convulsions NOS
- fits NOS
- seizures NOS

G41 **Status epilepticus**

G41.0 **Grand mal status epilepticus**

Tonic-clonic status epilepticus

Excl.: epilepsia partialis continua [Kozhevnikof] (G40.5)

G41.1 **Petit mal status epilepticus**

Epileptic absence status

G41.2 **Complex partial status epilepticus**

G41.8 **Other status epilepticus**

G41.9 **Status epilepticus, unspecified**

NLM

ICD-10 vs. ICD-10-CM

ICD-10

- G40 Epilepsy (10 codes)
- G41 Status epilepticus (5)

G40.4 Other generalized epilepsy and epileptic syndromes

Epilepsy with:
- myoclonic absences
- myoclonic-astatic seizures

Infantile spasms

Lennox-Gastaut syndrome

Salaam attacks

Symptomatic early West syndrome

ICD-10-CM

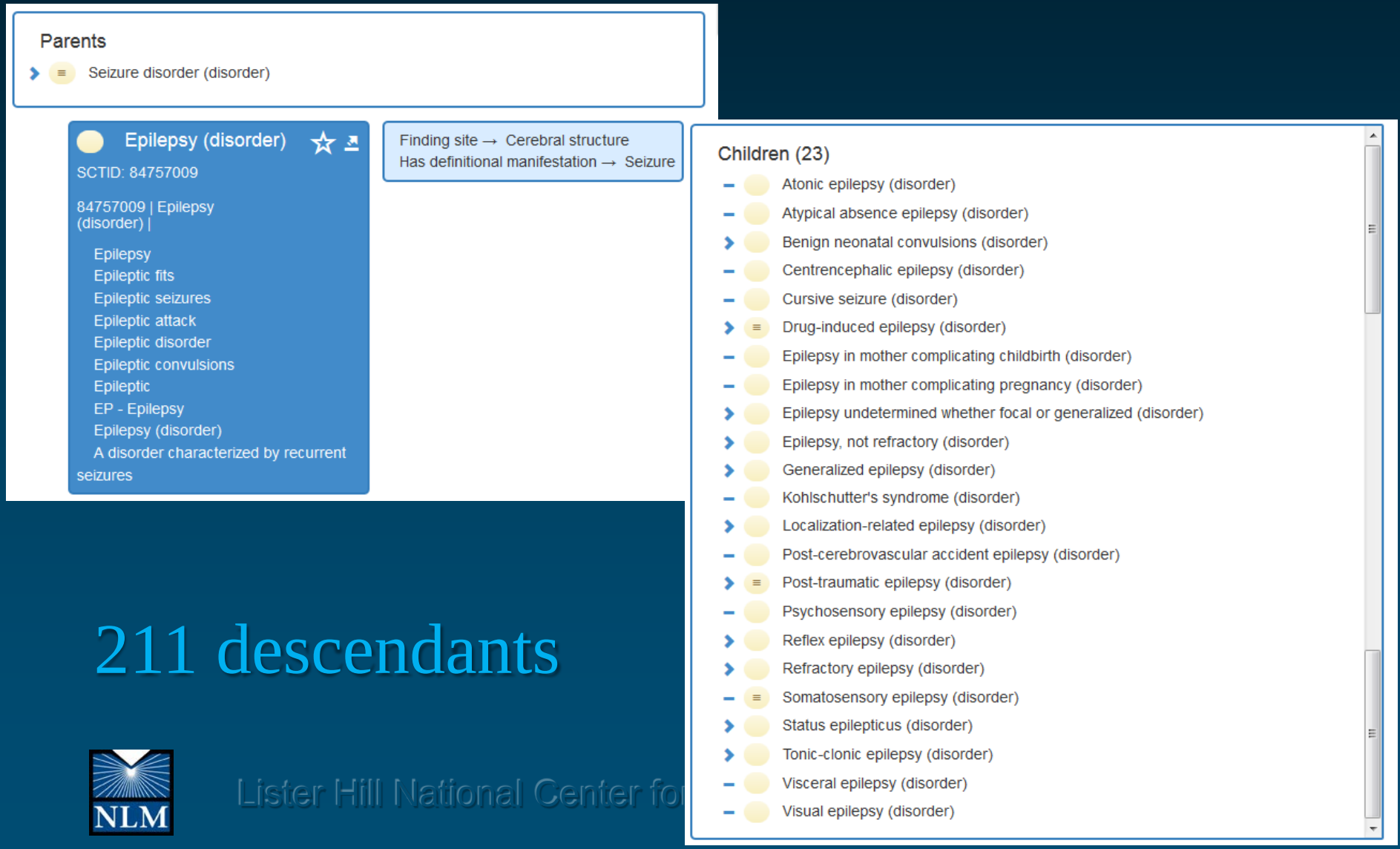
- G40 Epilepsy and recurrent seizures (77 codes)
- no G41
- Specific code(s) for
  - Rare forms
  - Tractability

G40.811	Lennox-Gastaut syndrome,	not intractable, with status epilepticus
G40.812	Lennox-Gastaut syndrome,	not intractable, without status epilepticus
G40.813	Lennox-Gastaut syndrome,	intractable, with status epilepticus
G40.814	Lennox-Gastaut syndrome,	intractable, without status epilepticus

http://browser.ihtsdotools.org/

SNOMED CT

ihtsdo Leading healthcare terminology, worldwide



211 descendants

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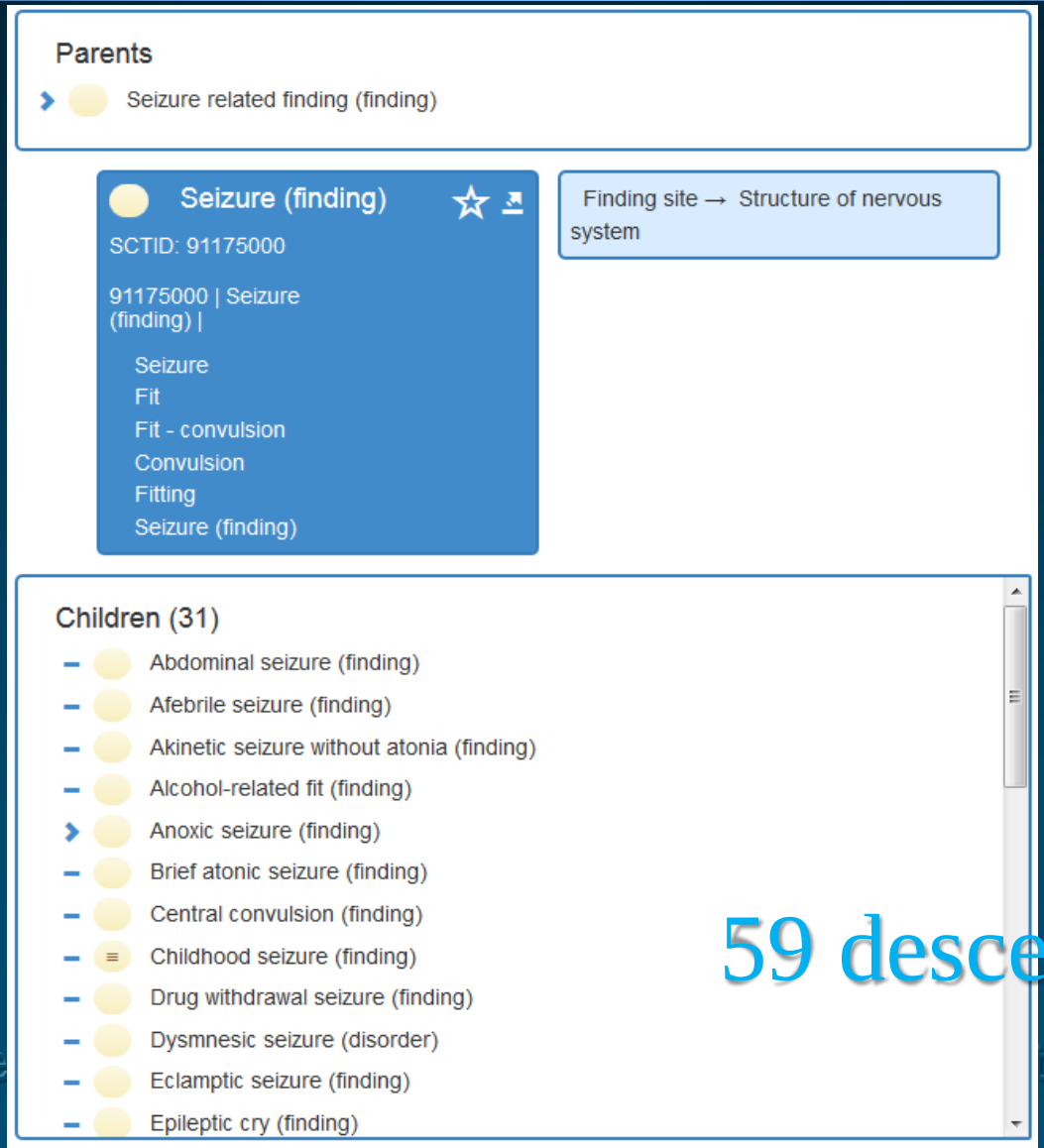
Lister Hill National Center for

SNOMED CT



59 descendants

https://search.loinc.org/

LOINC from Regenstrief

epilepsy

Search

LOINC	LongName	Component	Property	Timing	System	Scale	Method	exU
45424-9	Epilepsy [Minimum Data Set]	Epilepsy	Find	Pt	^Patient	Ord	MDS	
39080-7	EPM2A gene mutations found [Identifier] in Blood or Tissue by Molecular genetics method Nominal	EPM2A gene mutation analysis	Prid	Pt	Bld/Tiss	Nom	Molgen	
65366-7	Have you ever had, or has anyone ever told you that you had, a seizure disorder or epilepsy [PhenX]	Have you ever had, or has anyone ever told you that you had, a seizure disorder or epilepsy	Find	Pt	^Patient	Ord	PhenX	
62763-8	PhenX - epilepsy screener protocol	PhenX - epilepsy screener protocol	-	Pt	^Patient	-	PhenX	
38949-4	VA Compensation and Pension (C and P) examination epilepsy/narcolepsy	VA C&P exam.epilepsy &or narcolepsy note	Find	Pt	{Setting}	Doc	{Role}	
57909-4	ADNFLE gene mutations found [Identifier] in Blood or Tissue by Molecular genetics method Nominal	ADNFLE gene mutation analysis	Prid	Pt	Bld/Tiss	Nom	Molgen	
34490-3	MT-TK gene mutation analysis in Blood or Tissue by Molecular genetics method Narrative	MT-TK gene mutation analysis	Prid	Pt	Bld/Tiss	Nar	Molgen	
41082-9	MT-TK gene mutations found [Identifier] in Blood or Tissue by Molecular genetics method Nominal	MT-TK gene mutation analysis	Prid	Pt	Bld/Tiss	Nom	Molgen	
21713-3	MT-TK gene m.8344A>G [Presence] in Blood or Tissue by Molecular genetics method	MT-TK gene.m.8344A>G	Pr	Pt	Bld/Tiss	Ord	Molgen	
49631-5	ATN1 gene allele 1.CAG repeats [Entitic number] in Blood or Tissue by Molecular genetics method	ATN1 gene allele 1.CAG repeats	EntNum	Pt	Bld/Tiss	Qn	Molgen	{CAG
49632-3	ATN1 gene allele 2.CAG repeats [Entitic number] in Blood or Tissue by Molecular genetics method	ATN1 gene allele 2.CAG repeats	EntNum	Pt	Bld/Tiss	Qn	Molgen	{CAG
21756-2	ATN1 gene CAG repeats [Presence] in Blood or Tissue by Molecular genetics method	ATN1 gene.CAG repeats	Threshold	Pt	Bld/Tiss	Ord	Molgen	
40343-6	MT-TK gene m.8296A>G [Presence] in Blood or Tissue by Molecular genetics method	MT-TK gene.m.8296A>G	Pr	Pt	Bld/Tiss	Ord	Molgen	
40345-1	MT-TK gene m.8356T>C [Presence] in Blood or Tissue by Molecular genetics method	MT-TK gene.m.8356T>C	Pr	Pt	Bld/Tiss	Ord	Molgen	
40349-3	MT-TK gene m.8363G>A [Presence] in Blood or Tissue by Molecular genetics method	MT-TK gene.m.8363G>A	Pr	Pt	Bld/Tiss	Ord	Molgen	

https://search.loinc.org/

LOINC® from Regenstrief

seizure

Search

LOINC	LongName	Component	Property	Timing	System	Scale	Method
55427-9	Seizure disorder tracking panel	Seizure disorder tracking panel	-	Pt	^Patient	-	
66386-4	Has the child had a seizure or a brain problem [PhenX]	Has the child had a seizure or a brain problem	Find	Pt	^Patient	Ord	PhenX
65367-5	Have you ever had, or has anyone ever told you that you had, a seizure, convulsion, fit or spell under any circumstances [PhenX]	Have you ever had, or has anyone ever told you that you had, a seizure, convulsion, fit or spell under any circumstances	Find	Pt	^Patient	Ord	PhenX
70339-7	I am afraid of having a seizure - convulsion - in the past 7 days [FACIT]	I am afraid of having a seizure - convulsion - in the past 7D	Find	7D	^Patient	Ord	FACIT
65365-9	Did anyone ever tell you that you had a seizure or convulsion caused by a high fever when you were a child [PhenX]	Did anyone ever tell you that you had a seizure or convulsion caused by a high fever when you were a child	Find	Pt	^Patient	Ord	PhenX
65366-7	Have you ever had, or has anyone ever told you that you had, a seizure disorder or epilepsy [PhenX]	Have you ever had, or has anyone ever told you that you had, a seizure disorder or epilepsy	Find	Pt	^Patient	Ord	PhenX
66379-9	Have you had a seizure, brain, or other nervous system problem [PhenX]	Have you had a seizure, brain, or other nervous system problem	Find	Pt	^Patient	Ord	PhenX
32472-3	History of Seizure activity disorders	History of symptoms & diseases	Find	Pt	Seizure activity	Nom	Observed
60847-1	Seizure count Cerebral cortex Electroencephalogram (EEG)	Seizure count	Num	Procedure dur	Cerebral cortex	Qn	EEG
45662-4	Seizure disorder [Minimum Data Set]	Seizure disorder	Find	Pt	^Patient	Ord	MDS
74153-8	Seizure Disorder action plan	Seizure disorder action plan	Find	Pt	{Setting}	Doc	{Role}
54814-9	Seizure disorder in last 7 days [MDSv3]	Seizure disorder in last 7D	Find	7D	^Patient	Ord	MDSv3
55414-7	Seizures per month	Seizures per month	NRat	Pt	^Patient	Qn	
63822-1	When you stopped, cut down, or went without drinking, did you ever have fits, seizures, or convulsions, where you lost consciousness, fell to the floor, and had difficulty remembering what happened [PhenX]	When you stopped, cut down, or went without drinking, did you ever have fits, seizures, or convulsions, where you lost consciousness, fell to the floor, and had difficulty remembering what happened	Find	Pt	^Patient	Ord	PhenX

https://search.loinc.org/

65365-9 Did anyone ever tell you that you had a seizure or convulsion caused by a high fever when you were a child [PhenX]

NAME

Fully-Specified Name:

Component	Property	Time	System	Scale	Method
Did anyone ever tell you that you had a seizure or convulsion caused by a high fever when you were a child	Find	Pt	^Patient	Ord	PhenX

BASIC ATTRIBUTES

Class/Type:	PHENX/Clinical
Created On:	2011/04/29
Last Updated in Version:	2.44
Status:	Trial – caution, may change

NORMATIVE ANSWER LIST (LL1391-3)

SEQ#	Answer	Code	Answer ID
1	Yes	1	LA33-6
2	No	2	LA32-8
3	Possible	3	LA15097-1
4	Don't know	4	LA12688-0

SURVEY QUESTION

Text:	Did anyone ever tell you that you had a seizure or convulsion caused by a high fever when you were a child?
Source:	PhenX.130401010000

Generated from LOINC version 2.54.

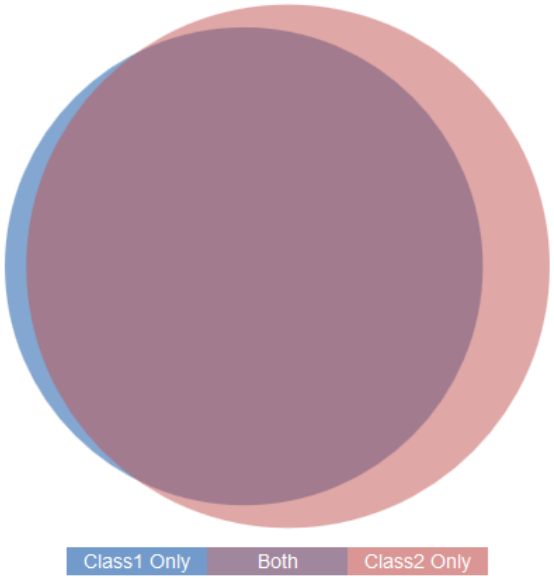
LOINC® from Regenstrief

55427-9 Seizure disorder tracking panel

PANEL HIERARCHY (view this panel in the LForms viewer)

LOINC#	LOINC Name	R/O/C	Cardinality	Ex. UCUM Units
55427-9	Seizure disorder tracking panel			
55414-7	Seizures per month	O		/mo
3432-2	Carbamazepine [Mass/volume] in Serum or Plasma	C		ug/mL
3487-6	Clobazam [Mass/volume] in Serum or Plasma	C		ug/mL
3494-2	Clonazepam [Mass/volume] in Serum or Plasma	C		ug/mL
3616-0	Ethosuximide [Mass/volume] in Serum or Plasma	C		ug/mL
6899-9	Felbamate [Mass/volume] in Serum or Plasma	C		ug/mL
9738-6	Gabapentin [Mass/volume] in Serum or Plasma	C		ug/mL
6948-4	Lamotrigine [Mass/volume] in Serum or Plasma	C		ug/mL
30471-7	Levetiracetam [Mass/volume] in Serum or Plasma	C		ug/mL
35331-8	Oxcarbazepine [Mass/volume] in Serum or Plasma	C		ug/mL
3948-7	Phenobarbital [Mass/volume] in Serum or Plasma	C		ug/mL
3968-5	Phenytoin [Mass/volume] in Serum or Plasma	C		ug/mL
47414-8	Pregabalin [Mass/volume] in Serum or Plasma	C		ug/mL
3978-4	Primidone [Mass/volume] in Serum or Plasma	C		ug/mL
21565-7	Tiagabine [Mass/volume] in Serum or Plasma	C		ug/mL
17713-9	Topiramate [Mass/volume] in Serum or Plasma	C		ug/mL
4086-5	Valproate [Mass/volume] in Serum or Plasma	C		ug/mL
30042-6	Vigabatrin [Mass/volume] in Serum or Plasma	C		ug/mL
29620-2	Zonisamide [Mass/volume] in Serum or Plasma	C		ug/mL

RxNorm / RxClass



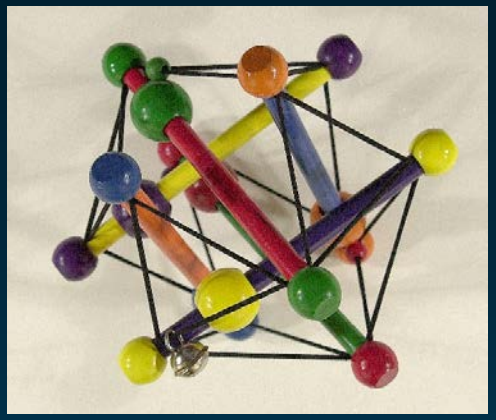
Class1: **ANTICONVULSANTS (N0000029145) in NDFRT (has_VAClass)**
Class2: **ANTIEPILEPTICS (N03A) in ATC**
Class1 Only: 1
Class2 Only: 6
Both: 24
Equivalence Score: 0.76
Inclusion Score: -0.69

RxNorm Name	RXCUI	Status
Carbamazepine	2002	Both
eslicarbazepine	1482502	Both
Ethosuximide	4135	Both
Ethotoin	4136	Both
ezogabine	1112990	Both
felbamate	24812	Both
gabapentin	25480	Both
lacosamide	623400	Both
lamotrigine	28439	Both
Levetiracetam	114477	Both
Mephenytoin	6757	Both
Mephobarbital	6758	Both
methsuximide	47858	Both
oxcarbazepine	32624	Both
perampanel	1356552	Both
Phenytoin	8183	Both
Primidone	8691	Both
rufinamide	69036	Both
tiagabine	31914	Both
topiramate	38404	Both
Trimethadione	10827	Both
Valproate	40254	Both
Vigabatrin	14851	Both
zonisamide	39998	Both
clobazam	21241	Class1 only
Brivaracetam	1739745	Class2 only
Clonazepam	2598	Class2 only
fosphenytoin	72236	Class2 only
Phenobarbital	8134	Class2 only
pregabalin	187832	Class2 only
sulthiame	10240	Class2 only

Beyond standard ontologies

Epilepsy ontologies

- Specialized ontologies
  - EpSO, ESSO
  - Finer-grained
  - Specific features (e.g., ILAE classification)
  - Useful for specific research studies/protocols
- But... unlikely to be used in mainstream EHR systems
  - Disconnect between healthcare and research
  - Limits secondary use of EHR data for epilepsy research
- Also consider extending standard ontologies (e.g., SNOMED CT) for better coverage of epilepsy



Medical Ontology Research

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Web: https://mor.nlm.nih.gov

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U.S. National Library of Medicine