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What is an ontology? (And why should you care?)

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Outline

- What is an ontology?
  - Definitions
  - Examples of biomedical ontologies
  - Applications of biomedical ontologies
- Why should you care?
  - EHR-based research
  - Promising ontology-enabled research
  - Do not reinvent the wheel!

What is an ontology?

Definition

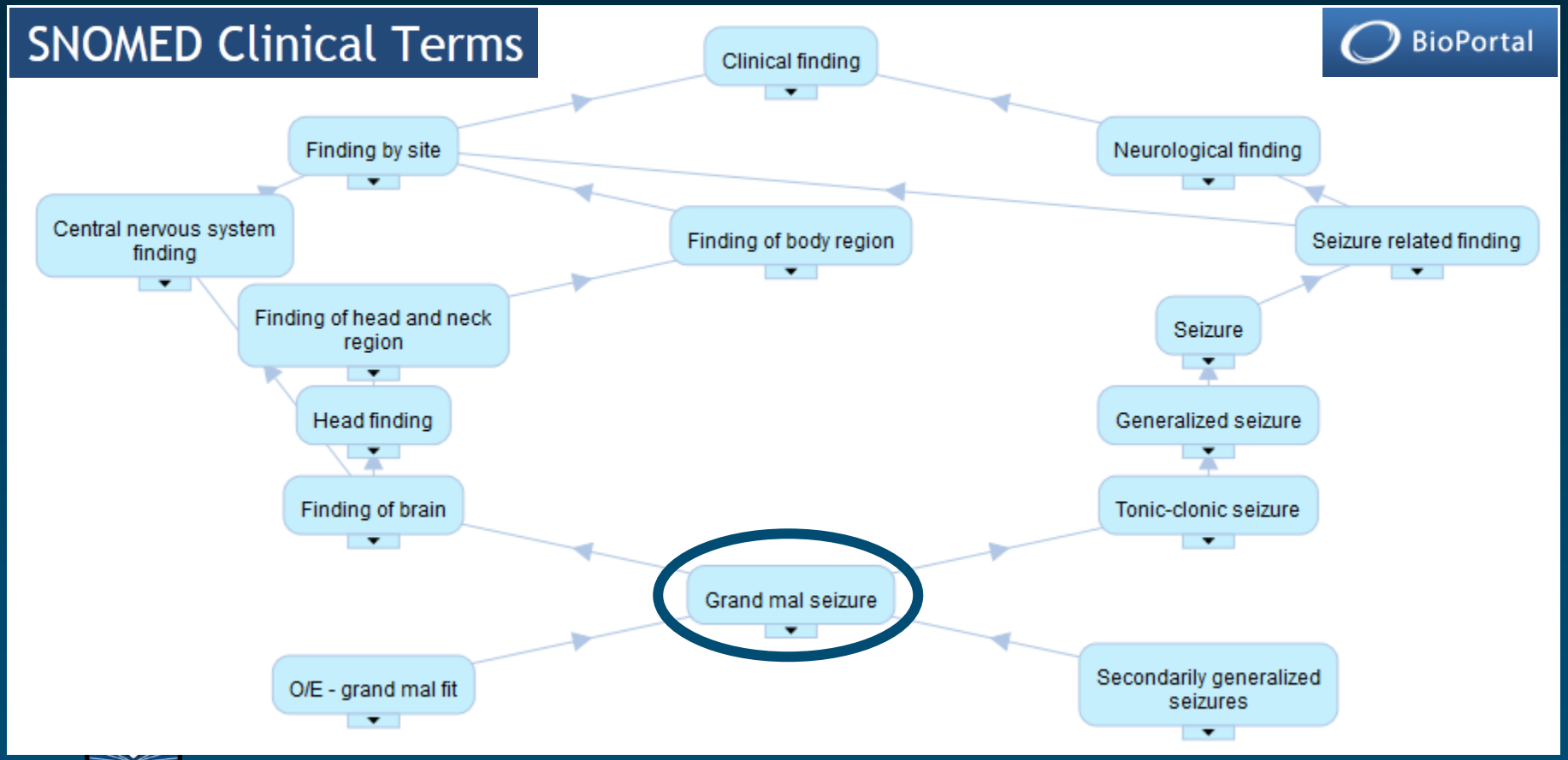
- Biomedical ontology
  - Artifact created for representing biomedical entities, their terms and their relations
- Ontology "spectrum"
  - Terminologies – focus on naming
  - Controlled vocabularies / Thesauri – focus on use for indexing and retrieval (knowledge organization)
  - Ontologies – support reasoning (logical definitions)
- Ontologies vs. knowledge bases
  - Definitional knowledge – mostly in ontologies
  - Assertional knowledge – mostly in knowledge bases

Example Vocabulary

- Vocabulary – Collection of terms
  - epileptic fit grand mal
  - generalized seizures tonic clonic
  - generalized tonic clonic seizure
  - generalized tonic-clonic seizure
  - Grand mal
  - Grand mal epileptic fit
  - Grand mal fit
  - Grand mal seizure
  - haut mal

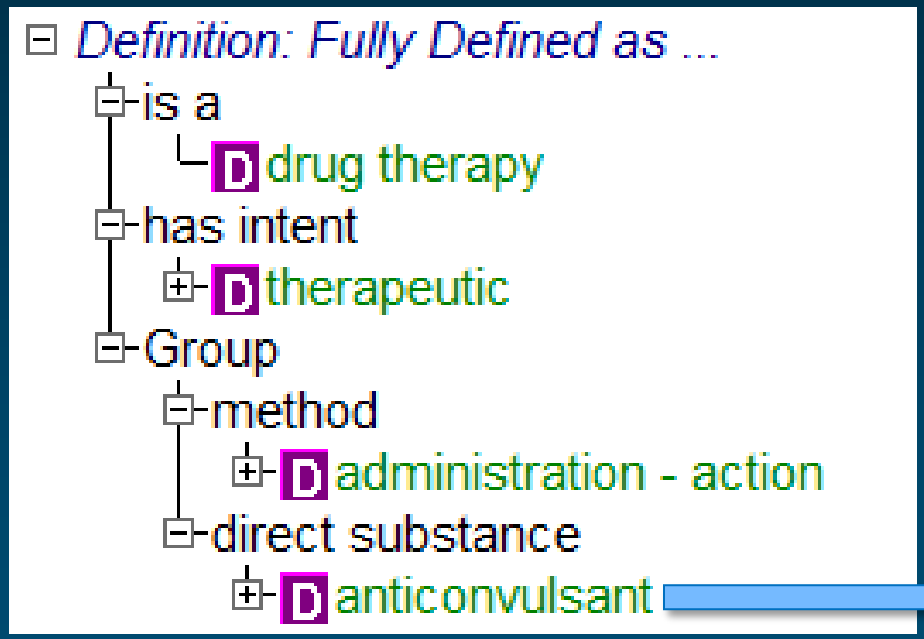
Example Relations

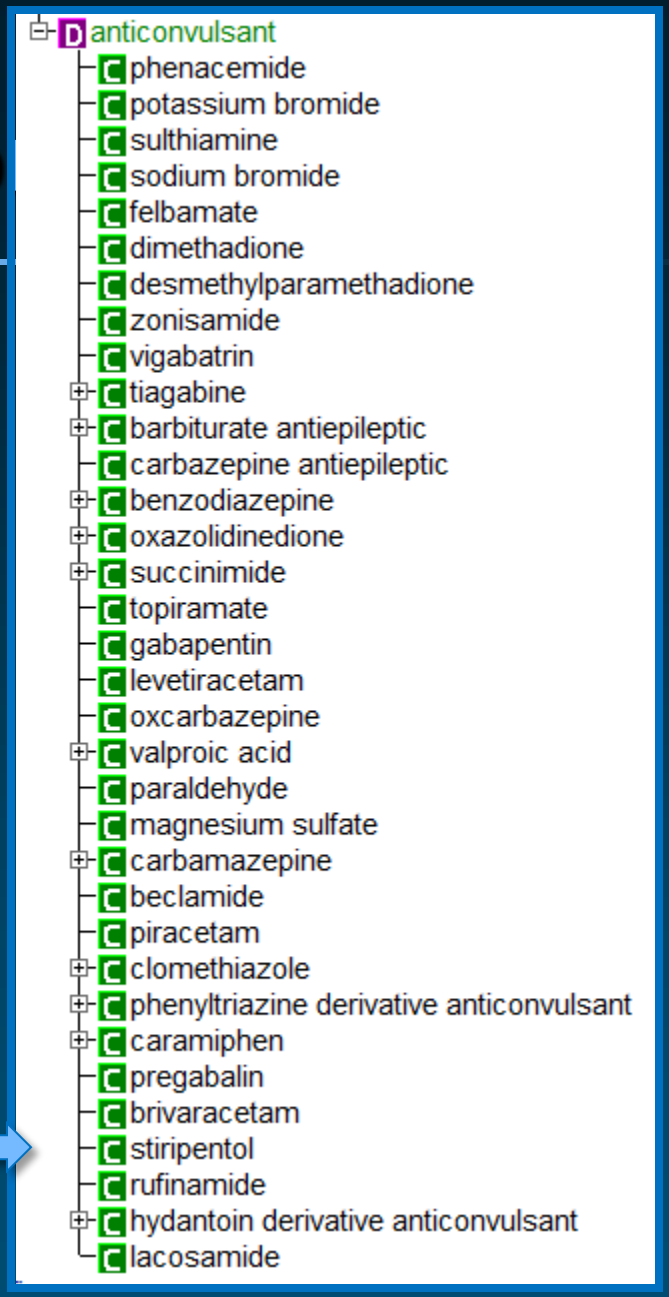
- Relations among entities



Example Logical definitio

- Anticonvulsivant therapy (in SNOMED CT)





Example Knowledge base

- Valproic acid (in NDF-RT)
  - National Drug File – Reference terminology

Kind	Subject	Predicate	
Drug	VALPROIC ACID	isa	V [Preparations]
Disease	VALPROIC ACID	CI_with	Drug Hypersensitivity
	VALPROIC ACID	CI_with	Liver Failure
	VALPROIC ACID	CI_with	Pregnancy
	VALPROIC ACID	may_treat	Alzheimer Disease
	VALPROIC ACID	may_treat	Bipolar Disorder
	VALPROIC ACID	may_treat	Epilepsy, Absence
	VALPROIC ACID	may_treat	Epilepsy, Complex Partial
Ingredient	VALPROIC ACID	has_Ingredient	Valproic Acid
Mechanism of Action	VALPROIC ACID	has_MoA	GABA A Receptor Interactions
	VALPROIC ACID	has_MoA	GABA B Receptor Interactions
Physiologic Effect	VALPROIC ACID	has_PE	Increased GABA Activity

3 examples of biomedical ontologies

- International Classification of Diseases (ICD)
- SNOMED Clinical Terms (SNOMED CT)
- Medical Subject Headings (MeSH)

International Classification of Diseases

ICD Characteristics (1)

- Current version: ICD-10
- Type: Classification
- Domain: Disorders
- Developer: World Health Organization (WHO)
- Funding: WHO
- Availability
  - Publicly available: No
  - Repositories: UMLS and BioPortal
- URL: http://www.who.int/classifications/icd/en/

ICD Characteristics (2)

- Number of
  - Concepts: 12,318
  - Terms: 1 per concept (tabular)
- Major organizing principles:
  - Tree (single inheritance hierarchy)
  - No explicit classification criteria
    - Idiosyncratic inclusion/exclusion mechanism
  - .8 slots for Not elsewhere classified (NEC)
  - .9 slots for Not otherwise specified (NOS)
- Formalism: Proprietary format

ICD Top level

- ICD-10 Version:2010
  - 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
  - VII Diseases of the eye and adnexa
  - VIII Diseases of the ear and mastoid process
  - IX Diseases of the circulatory system
  - X Diseases of the respiratory system
  - XI Diseases of the digestive system
  - XII Diseases of the skin and subcutaneous tissue
  - XIII Diseases of the musculoskeletal system and connective tissue
  - XIV Diseases of the genitourinary system
  - XV Pregnancy, childbirth and the puerperium
  - XVI Certain conditions originating in the perinatal period
  - XVII Congenital malformations, deformations and chromosomal abnormalities
  - XVIII Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
  - XIX Injury, poisoning and certain other consequences of external causes
  - XX External causes of morbidity and mortality
  - XXI Factors influencing health status and contact with health services
  - XXII Codes for special purposes

Epilepsy in ICD-10 (1)

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's 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

Epilepsy in ICD-10 (2)

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's 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

SNOMED Clinical Terms

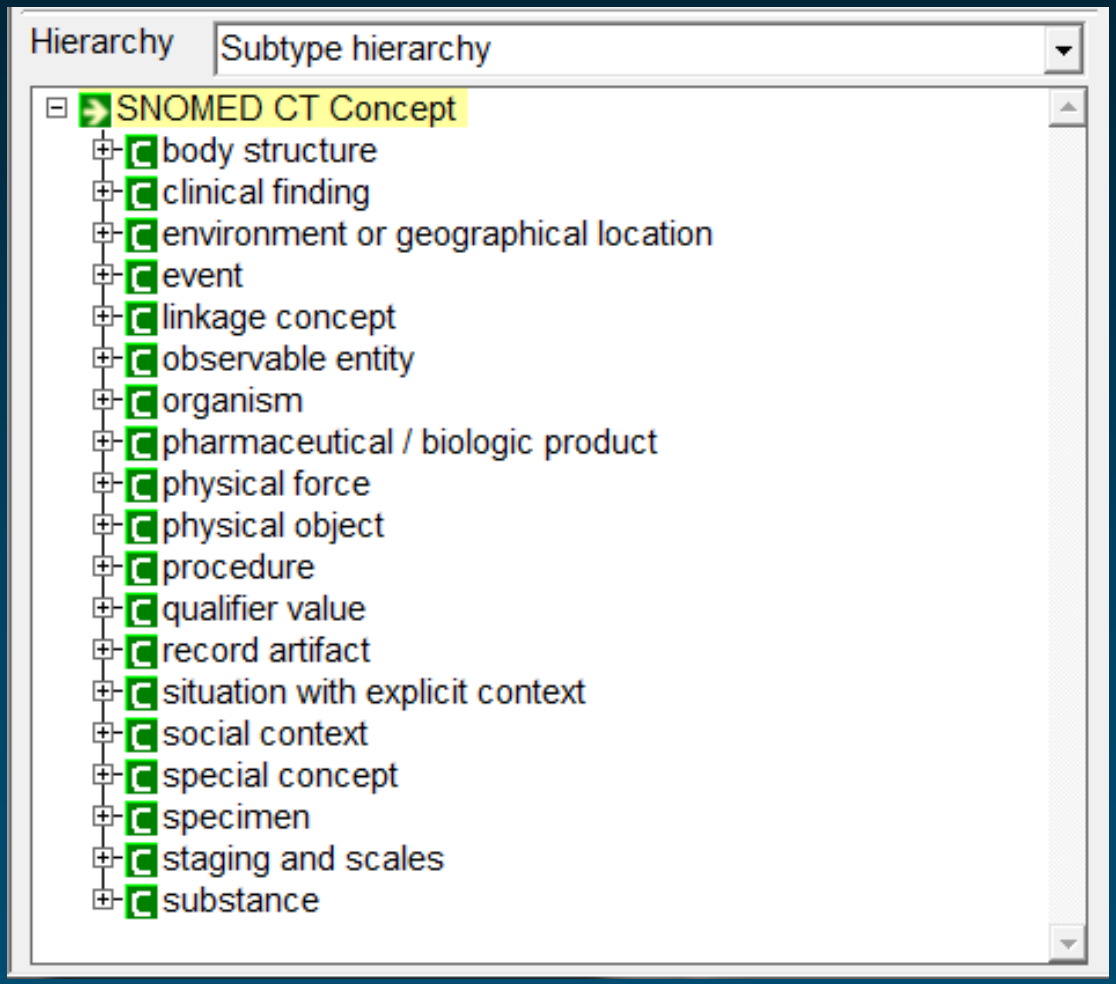
SNOMED CT Characteristics (1)

- Current version: July 31, 2012 (2 annual releases)
- Type: Reference terminology / ontology
- Domain: Clinical medicine
- Developer: IHTSDO
- Funding: IHTSDO
- Availability
  - Publicly available: Yes* (in member countries)
  - Repositories: UMLS
- URL: http://www.ihtsdo.org/

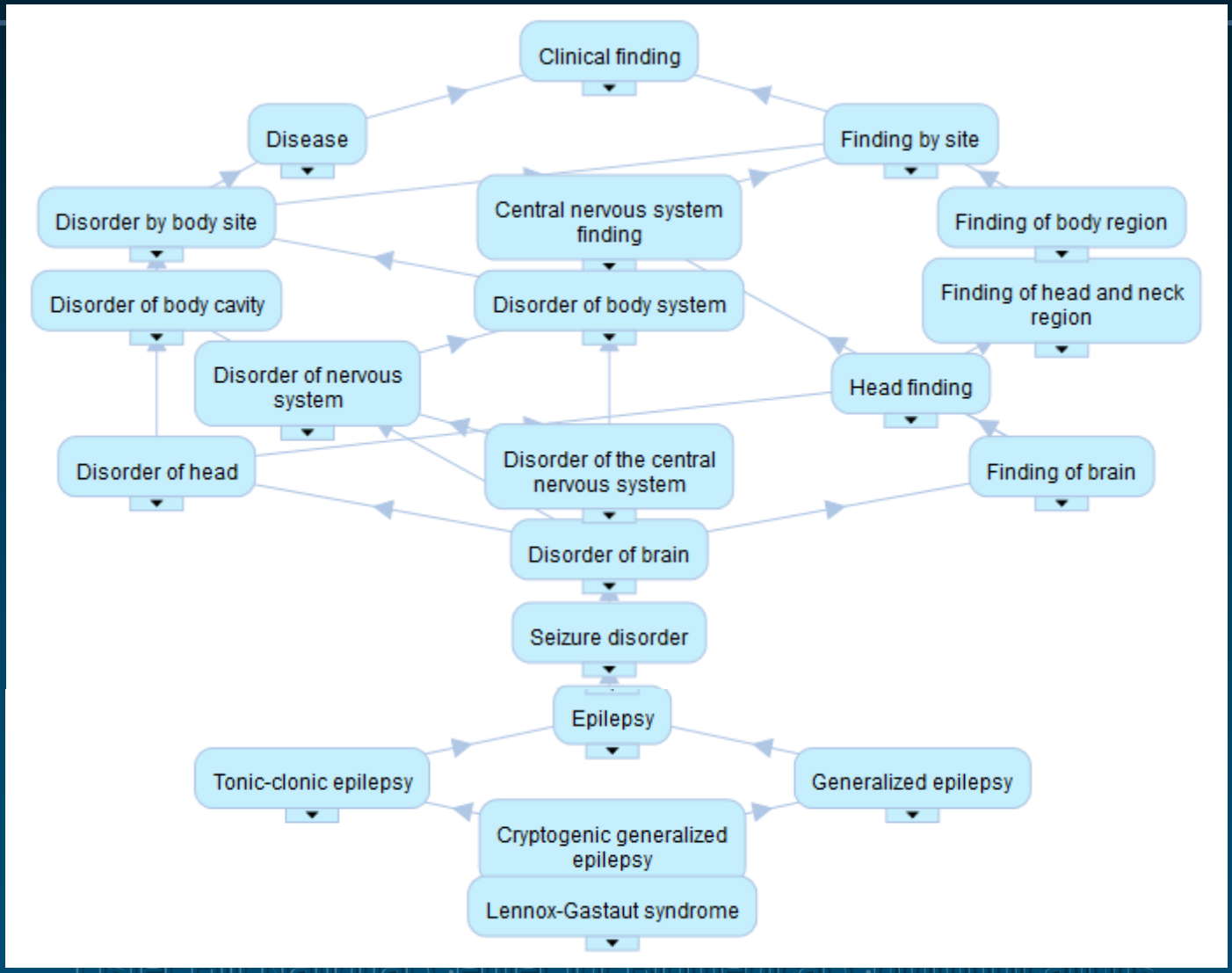
SNOMED CT Characteristics (2)

- Number of
  - Concepts: ~300,000 active concepts (July 31, 2012)
  - Terms: ~1M active "descriptions"
- Major organizing principles:
  - Utility for clinical medicine (e.g., assertional + definitional knowledge)
  - Model of meaning (incomplete)
  - Rich set of associative relationships
  - Small proportion of defined concepts (many primitives)
- Formalism: Description logics (KRSS)

SNOMED CT Top level



Epilepsy in SNOMED CT



Medical Subject Headings (MeSH)

MeSH Characteristics (1)

- Current version: 2012 (yearly releases)
- Type: Thesaurus / Controlled vocabulary
- Domain: Biomedicine
- Developer: NLM
- Funding: NLM (Library Operations)
- Availability
  - Publicly available: Yes
  - Repositories: UMLS / NCBO BioPortal
- URL: http://www.nlm.nih.gov/mesh/

MeSH Characteristics (2)

- Number of
  - Concepts: 26,581 descriptors (2012)
  - Terms: 7.5 per descriptor
- Major organizing principles:
  - Descriptor + entry terms
    (also: Qualifiers, Supplementary concepts)
  - Thesaurus relations (RB/RN/RO)
- Formalism: Thesaurus / Proprietary XML DTD

MeSH Top level

1. Anatomy [A]
2. Organisms [B]
3. Diseases [C]
4. Chemicals and Drugs [D]
5. Analytical, Diagnostic and Therapeutic Techniques and Equipment [E]
6. Psychiatry and Psychology [F]
7. Biological Sciences [G]
8. Natural Sciences [H]
9. Anthropology, Education, Sociology and Social Phenomena [I]
10. Technology, Industry, Agriculture [J]
11. Humanities [K]
12. Information Science [L]
13. Named Groups [M]
14. Health Care [N]
15. Publication Characteristics [V]
16. Geographicals [Z]

MeSH Example (terms)

MeSH Heading	Epilepsy
Tree Number	C10.228.140.490
Annotation	GEN or unspecified; prefer specifics
Scope Note	A disorder characterized by recurrent episodes of paroxysmal brain dysfunction due to a sudden, disorderly, and excessive neuronal discharge. Epilepsy classification systems are generally based upon: (1) clinical features of the seizure episodes (e.g., motor seizure), (2) etiology (e.g., post-traumatic), (3) anatomic site of seizure origin (e.g., frontal lobe seizure), (4) tendency to spread to other structures in the brain, and (5) temporal patterns (e.g., nocturnal epilepsy). (From Adams et al., Principles of Neurology, 6th ed, p313)
Entry Term	Aura
Entry Term	Awakening Epilepsy
Entry Term	Epilepsy, Cryptogenic
Entry Term	Epileptic Seizures
Entry Term	Seizure Disorder
Entry Term	Seizures, Epileptic
Entry Term	Single Seizure
See Also	Seizures
Allowable Qualifiers	BL CF CI CL CN CO DH DI DT EC EH EM EN EP ET GE HI IM
Date of Entry	19990101
Unique ID	D004827

Name of Substance	Epileptic encephalopathy, Lennox-Gastaut type
Record Type	C
Registry Number	0
Entry Term	Encephalopathy of childhood
Entry Term	Lennox-Gastaut syndrome
Heading Mapped to	*Intellectual Disability
Heading Mapped to	*Spasms, Infantile
Frequency	65
Date of Entry	20100825
Unique ID	C535500

MeSH Example (hierarchies)

Nervous System Diseases [C10]
- Central Nervous System Diseases [C10.228]
  - Brain Diseases [C10.228.140]
    - Epilepsy [C10.228.140.490]
      - Epilepsies, Myoclonic [C10.228.140.490.250] +
      - Epilepsies, Partial [C10.228.140.490.360] +
      - Epilepsy, Benign Neonatal [C10.228.140.490.370]
      - ▶ Epilepsy, Generalized [C10.228.140.490.375]
        - Epilepsy, Absence [C10.228.140.490.375.260]
        - Epilepsy, Tonic-Clonic [C10.228.140.490.375.290]
        - Spasms, Infantile [C10.228.140.490.375.760]
      - Epilepsy, Post-Traumatic [C10.228.140.490.380]
      - Epilepsy, Reflex [C10.228.140.490.450]
      - Landau-Kleffner Syndrome [C10.228.140.490.535]
      - Seizures [C10.228.140.490.631]
      - Seizures, Febrile [C10.228.140.490.650]
      - Status Epilepticus [C10.228.140.490.690] +

Applications of biomedical ontologies

- 3 major categories of use [Bodenreider, YBMI 2008]
  - Knowledge management (indexing and retrieval of data and information, access to information, mapping among ontologies)
  - Data integration, exchange and semantic interoperability
  - Decision support and reasoning (data selection and aggregation, decision support, natural language processing applications, knowledge discovery).

Applications Knowledge management

- Source of vocabulary and definitions for
  - Annotation (e.g., text mining)
  - Indexing (and information retrieval)
  - Coding (clinical records, registries)
- Source of mapping across ontologies
  - Correspondence between terms across ontologies
  - Terminology integration systems
    - Unified Medical Language System
    - BioPortal

Applications Interoperability

- Exchange of standardized data
  - Use of standard vocabularies and protocols
  - E.g., HL7 messages, clinical documents (CDA)
- Data integration
  - Clinical data warehouses (for translational research)
    - Data standardized while loading
  - Query translation against federated data repositories
    - Supported by ontologies

Applications Decision support / reasoning

- Hierarchical information in ontologies helps bridge across levels of granularity
  - CDS rule expressed at the level of a pharmacologic class
    - E.g., interactions between anti-convulsivants and other drugs
  - Cohort selection
    - Retrieve all patients admitted for seizure
  - Hypothesis generation / Knowledge discovery
    - Aggregate relations to increase statistical power (e.g., aggregate drugs at the level of pharmacologic class in relation to adverse events)

Why should you care?

3 reasons why you should care

- EHR-based research
- Promising ontology-enabled research
- Do not reinvent the wheel!

EHR-based research

- Clinical data warehouses
  - Secondary use of clinical data
  - Provide large amounts of data
    - Much larger than regular clinical trials
  - Integration of clinical data across institutions
    - When standardized
- Enable new forms of clinical research
  - Translational research
    - Integration with genomic data
  - Study of adverse events based on observational data
    - Post-marketing surveillance of drugs
  - "Learning Healthcare System"
    - EHR data become knowledge

Promising ontology-enabled research

- Basic ingredients
  - Vocabulary from ontologies is used to standardize mentions of biomedical entities in a corpus (MEDLINE articles, EHR data)
    - Term extraction systems (natural language processing)
  - Ontological relations are used to aggregate semantically similar datapoints in order to increase statistical power
    - Clustering based on semantic similarity
  - Data mining techniques are used to identify novel, salient relations among biomedical entities

Do not reinvent the wheel!

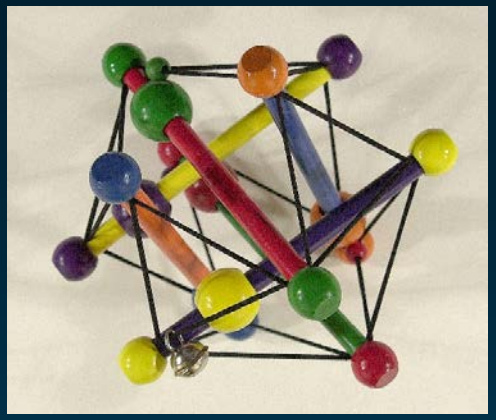
- Leverage existing ontologies (for annotation, aggregation, etc.)
  - Jump on the “standards” bandwaggon
- Ontology development is difficult and expensive
  - Be clinicians / researchers; collaborate with ontologists
- There are already many clinical ontologies available
  - Basic research must follow the same standards as clinical research to become “translational”

References

- Bodenreider O. Biomedical ontologies in action: role in knowledge management, data integration and decision support. Yearb Med Inform. 2008:67-79.
  PubMed PMID: 18660879; PubMed Central PMCID: PMC2592252
- Cimino JJ, Zhu X. The practical impact of ontologies on biomedical informatics. Yearb Med Inform. 2006:124-35.
  PubMed PMID: 17051306

Resources

- Unified Medical Language System (UMLS)
  - National Library of Medicine
  - https://uts.nlm.nih.gov/
- BioPortal
  - National Center for Biomedical Ontology
  - http://bioportal.bioontology.org/
- Open Biomedical Ontology
  - OBO Community
  - http://www.obofoundry.org/



Medical Ontology Research

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