How Ontologies can Improve Semantic Interoperability in Health Care

KR4HC – ProHealth'13
Murcia, Spain, June 1st, 2013
"... integrating resources that were developed using different vocabularies and different perspectives on the data. To achieve semantic interoperability, systems must be able to exchange data in such a way that the precise meaning of the data is readily accessible and the data itself can be translated by any system into a form that it understands."

"... integrating resources that were developed using different **vocabularies** and different **perspectives** ... "

- **"Vocabularies":** Terminologies / classifications / ontologies
  - Provide codes that denote types of clinical entities (84114007 | heart failure |): ICD, SNOMED CT.

- **"Perspectives":** EHR information models
  - Provide standardized structure (section, entry, cluster, etc.) and context (past history, order, ...) for clinical data: openEHR, ISO 13606, HL7 CDA.
"Vocabularies": Terminologies / classifications / ontologies

- Provide codes that denote types of clinical entities (84114007 |heart failure|): ICD, SNOMED CT.

**Current Concept:**
Malignant tumor of breast (disorder)

**Parent(s):**
- Malignant neoplasm of thorax (disorder)
- Neoplasm of breast (disorder)

**Child(ren):**
(N=14) Select a child to make it to the "Current Concept"
- Carcinoma of breast (disorder)
- Familial cancer of breast (disorder)
- Hormone receptor positive malignant neoplasm of breast (disorder)
- Local recurrence of malignant tumor of breast (disorder)
- Malignant lymphoma of breast (disorder)
- Malignant melanoma of breast (disorder)
- Malignant neoplasm of auxiliary tail of breast (disorder)
- Malignant neoplasm of breast lower inner quadrant (disorder)
- Malignant neoplasm of breast lower outer quadrant (disorder)
- Malignant neoplasm of breast upper inner quadrant (disorder)
- Malignant neoplasm of breast upper outer quadrant (disorder)
- Malignant neoplasm of female breast (disorder)
- Malignant neoplasm of male breast (disorder)
- Primary malignant neoplasm of breast (disorder)
- Sarcoma of breast (disorder)

**Defining Relationships:**
- Is a Malignant neoplasm of thorax (disorder)
- Is a Neoplasm of breast (disorder)

**Group 1**
**Associated morphology**
Malignant neoplasm of primary, secondary, or uncertain origin (morphologic abnormality)
Breast structure (body structure)

**Finding site**
This concept is fully defined.

**Qualifiers:**
- View Qualifying Characteristics and Facts

**Descriptions (Synonyms):**
- Fully Specified Name: Malignant tumor of breast (disorder)
- Preferred: Malignant tumor of breast [379661016]
- Synonym: Breast cancer [379662011]
- Synonym: CA - Breast cancer [379663018]
- Preferred: Malignant tumour of breast [379664012]

**Related Concepts:**
- All "Is a" antecedents -
- All descendents/subtypes -
- Related concepts demo -

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Semantic Standards

- "Vocabularies": Terminologies / classifications / ontologies
  - Provide codes that denote types of clinical entities (84114007 | heart failure|): ICD, SNOMED CT.

- "Perspectives": EHR information models
  - Provide standardized structure (section, entry, cluster, etc.) and context (past history, order, ...) for clinical data: openEHR, ISO 13606, HL7 CDA.

```plaintext
SECTION[at0000] matches { -- History of problem / condition
members cardinality matches {1..*; unordered} matches {
ENTRY[at0001] matches { -- Problem / Condition
items cardinality matches {1..*; unordered } matches {
ELEMENT[at0002] matches { -- Diabetes Mellitus
value matches {
SIMPLE_TEXT[at0003] matches { -- SIMPLE_TEXT
originalText matches {"Yes","No","Unknown"}
}
}
}...})}
```
Semantic Standards

- **"Vocabularies":** Terminologies / classifications / ontologies
  - Provide codes that denote types of clinical entities
    (84114007 | heart failure |): ICD, SNOMED CT.

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  - Provide standardized structure (section, entry, cluster, etc.) and context (past history, order, ...) for clinical data:
    openEHR, ISO 13606, HL7 CDA.

Heart failure diagnosis confirmed

Terminology class/concept

Information entity

Need for detecting iso-semantic expressions!!!
Overlap Terminologies / Information Models

- Clinical Terminologies
  - Terminologies to be used without information models

- Clinical Information Models
  - Clinical Information models to be used without or with inexpressive terminologies
  - Contextual statements (negation, plans, beliefs...) within terminologies
    - SNOMED CT context model
    - ICD 11 content model
  - Local terminology within IMs
  - Postcoordination within IMs
The same meaning is represented by...

"Suspected heart failure caused by ischaemic heart disease"

"Finding with explicit context" and DueTo some "Ischaemic heart disease" and FindingContext some "Suspected"

Diagnosis:  "Heart Failure"
Certainty:  "Suspected"
Etiology:  "Ischaemic heart disease"
SemanticHealthNet will develop a scalable and sustainable pan-European organisational and governance process for the semantic interoperability of clinical and biomedical knowledge, to help ensure that EHR systems are optimised for patient care, public health and clinical research across healthcare systems and institutions.

Through a clinically-driven workplan, exemplified in cardiovascular medicine, SemanticHealthNet will capture the needs for evidence-based, patient-centred integrated care and for public health, encapsulating existing European consensus in the management of chronic heart failure and cardiovascular prevention. Experts in EHR architectures, clinical data structures, terminologies and ontology will combine, tailor and pilot their best-of-breed resources in response to the needs articulated by clinicians and public health physicians.

These exemplars will be cross-referenced with other domains and stakeholder perspectives via Clinical and Industrial Advisory Boards and interactions with other projects in Topic 5.3. The project will generalise and formalise the methods and best practices in how to combine and adapt informatics resources to support semantic interoperability, and how these can be developed and supported at scale. Health authorities, clinical professionals, ministries, vendors, purchasers, insurers are involved to ensure the project approach and results are realistically adoptable and viable, building on the SemanticHEALTH and CALLIOPE roadmaps.

A business model to justify strategic investments, including the opportunity costs for key stakeholders such as SDOs, industry, will be defined. This, and links with epSOS II and the eHealth Governance Initiative, will inform the shape of the Virtual Organisation that this Network will establish to sustain semantic interoperability developments and their adoption.

The consortium comprises more than 40 internationally recognised experts, including from USA and Canada, ensuring a global impact.
Challenge of SemanticHealthNet NoE

- Create interoperability between isosemantic but heterogeneous representations of structured clinical content
- Target: optimise clinical queries and exchange of data
- Method: Formal ontologies and description logics (OWL DL)

<table>
<thead>
<tr>
<th>Organ Failure Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organ</strong></td>
</tr>
<tr>
<td><strong>Status</strong></td>
</tr>
<tr>
<td><strong>Caused by ischaemic heart disease</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
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<td><strong>Status</strong></td>
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<tr>
<td>Suspected</td>
</tr>
<tr>
<td><strong>Cause</strong></td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
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</table>
Semantic interoperability by ontology annotations

Stefan Schulz: How Ontologies can Improve Semantic Interoperability in Health Care
Ontologies for SemanticHealthNet

COMMON ONTOLOGY STRUCTURE & TERMINOLOGY

Top-level ontology

Information entity ontology

Domain Ontology (SNOMED CT)
Different views on (formal) ontologies

- **Computer science view**
  - Ontologies are purpose-oriented formal models of meaning (conceptualizations)

- **Cognitive / linguistic view**
  - Ontologies are concept systems or systems of semantic reference (no clear distinction from thesauri)
  - Also adopted by parts of the Semantic Web community
  - Not clearly distinguished from knowledge representation in general

- **Philosophy view (scientific realism)**
  - Ontology is the study of what there is
  - Formal Ontologies give precise mathematical formulations of the properties and relations of certain entities.

Basic principles we subscribe to

- Ontologies as formal systems (using appropriate language)
- Ontological commitment supported by
  - disjoint upper-level categories (process, object, ...)
  - closed set of basic relations
  - constraining axioms
- Clear division between classes and individuals
- Equivalence and Subsumption statements
- Aristotelian definitions (genus – differentia)
- Naming conventions
- Design patterns und guidelines

→ towards "evidence-based" ontology engineering
Class-individual distinction not discretionary

Every human is a primate, every primate is a vertebrate
→ Every human is a vertebrate

A subClassOf B
iff
∀a:A(a) → B(a)

Human subClassOf Primate
Intuitive taxonomies $\neq$ good taxonomies

Test:
• there is no neoplasms that is not an oncology
• there is no prostate that is not a neoplasms
• there is no oncology that is not a clinical medicine
Stefan Schulz: How Ontologies can Improve Semantic Interoperability in Health Care

Intuitive taxonomies $\neq$ good taxonomies

$\forall a: A(a) \rightarrow B(a) \iff \neg \exists a: A(a) \land \neg B(a)$

Test:
- oncology is an instance of a medical discipline
- there is no prostate neoplasm that is not a neoplasm

Labelling!

http://en.wikipedia.org/wiki/OntoClean
Aristotelian Definitions do not permit exceptions

FOL: \( \forall x: \text{Hepatitis}(x) \leftrightarrow \text{ViralInfection}(x) \land \exists \text{Liver} : C(z) \land \text{hasLocus}(x,z) \)

OWL-DL: \( \text{ViralHepatitis} \text{equivalentTo} \text{ViralInfection} \text{and} \text{hasLocus some Liver} \)

Test:
- There is no viral hepatitis that is not located in a liver
- There is no viral hepatitis that is not a viral infection
Always investigate the ontological commitment

- Which are exactly the instances?
- Does the label tell us what is meant?
- Is there an implicit context?

Test:

- There is no neoplasm in both lungs that is not a neoplasm in the left lung OR There is no patient with neoplasm in both lungs that is not a patient with the neoplasm in the left lung
- There is no varicose vein in the lower limb that is not a chronic peripheral venous insufficiency OR There is no patient with varicose lower limb veins that is not a patient with a chronic peripheral venous insufficiency
Upper level ontologies partition the domain into disjoint and exhaustive categories

- Upper level ontologies enforce a strict categorization
- Constraints on upper-level categories
- Upper level ontology for the biomedical domain **BioTop**
BioTopLite provides a small set of toplevel classes, relations, and axioms

- Precise formulations about generic and defining properties of basic categories of a domain
- Logical Framework (Description logics)
- OWL – DL (Web Ontology Language) complete and decidable language - compromise between expressiveness and performance (EXPTIME)

Automated reasoning enables checking consistency, equivalence and subsumption

Ontologies play an increasing role in new generation of biomedical terminology systems

Toplevel Categories

- Precise formulations about generic and defining properties of basic categories of a domain
- Logical Framework (Description logics)
- OWL – DL (Web Ontology Language) complete and decidable language - compromise between expressiveness and performance (EXPTIME)

Automated reasoning enables checking consistency, equivalence and subsumption

Ontologies play an increasing role in new generation of biomedical terminology systems

Elena Beißwanger, Stefan Schulz, Holger Stenzhorn and Udo Hahn
Ontology development should be guideline-based

Guideline on Developing Good Ontologies in the Biomedical Domain with Description Logics

URL: http://www.purl.org/googod/guideline

Version 1.0
December 2012

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11th December 2012

http://purl.org/googod/guideline
Formal ontologies vs. human conceptualizations

- Built around taxonomies of classes
  - ATTENTION: our intuitive way of hierarchically organize terms is not strictly taxonomic (e.g. Anatomy)
- State what is true for all individual members of a class (instances of a type)
- Requires to distinguish between classes and individuals
  - ATTENTION: human language is often misleading, e.g. "London is a big city" vs. "The liver is a big organ"
- Individuals commit to upper-level categories
  - ATTENTION: our thinking fuses mutually dependent entities that belong to different categories, e.g. Cancer (growth process vs. mass of malignant tissue)
- Upper level categories should be made explicit
  - Explicit upper level ontology – common understanding
  - Implicit upper level ontology of each of us – misunderstanding
Beware of creating "Nontologies"

- OWL syntax without description logics semantics
- Formal reasoning leads to incorrect entailments
- Examples: NCI thesaurus, Radlex
- Many other ontologies contain problematic axioms that contradict the intended meaning
- Example (NCI thesaurus):

  \[
  \text{Calcium-Activated}\_\text{Chloride}\_\text{Channel-2} \ \text{subClassOf} \\
  \quad \text{Gene}\_\text{Product}\_\text{Expressed}\_\text{In}\_\text{Tissue} \ \text{some} \ Lung \ \text{and} \\
  \quad \text{Gene}\_\text{Product}\_\text{Expressed}\_\text{In}\_\text{Tissue} \ \text{some} \ Mammary\_\text{Gland} \ \text{and} \\
  \quad \text{Gene}\_\text{Product}\_\text{Expressed}\_\text{In}\_\text{Tissue} \ \text{some} \ Trachea \\
  \]

  \[
  \text{Ureter}\_\text{Small}\_\text{Cell}\_\text{Carcinoma} \ \text{subclassOf} \\
  \quad \text{Disease}\_\text{May}\_\text{Have}\_\text{Finding} \ \text{some} \ Pain
  \]

Schulz S, Schober S, Tudose I, Stenzhorn H: The Pitfalls of Thesaurus Ontologization – the Case of the NCI Thesaurus. AMIA Annu Symp Proc, 2010: 727-731
Large parts of knowledge are not ontological

- Ontology ≠ Knowledge representation
  - "There are very few interesting items of knowledge that are truly ontological in this strict sense" (Alan Rector)
  - antinomy: ὄντος (being → ontology) vs. ἐπιστήμη (knowledge → epistemology)

- Ontology is not appropriate for
  - Default knowledge
    - "The hand has 5 fingers" (unless otherwise stated)
  - Probabilistic knowledge
    - Mesothelioma is a rare cancer
  - Contingent knowledge
    - Aspirin prevents myocardial infarction
    - Jaundice is a typical symptom of hepatitis

Can ontology represent clinical information?

Can formal ontology represent both information and clinical information?

Clinical Terminologies

Clinical Information Models
Ontologies used and created in SemanticHealthNet

- Meaning of medical terms / concepts
- Clinical Processes
- Information Artifacts
Ontologies used and created in SemanticHealthNet

- Meaning of medical terms / concepts
- Clinical Processes
- Information Artifacts
- SNOMED CT Domain Ontology
Ontologies used and created in SemanticHealthNet

- Meaning of medical terms / concepts
- Clinical Processes
- Information Artifacts
- SNOMED CT Domain Ontology
- BioTopLite Upper Level Ontology
Basic representational pattern for terminology binding

- Example: Diagnosis (statement about clinical condition)

Demographics
Time stamps
Metadata

Patient X
Basic representational pattern for terminology binding

Example: Diagnosis (statement about clinical condition)

InformationEntity and hasQuality InformationItemQuality and isAboutSituation only (ClinicalSituation and ...)

EHR
- WHAT?
- WHO?
- WHEN?

Neoplasia

OWL annotation of an information item
Example:
“Suspected heart failure caused by ischaemic heart disease”
Example:
“Suspected heart failure caused by ischaemic heart disease”

- One code or postcoordinated expression in SNOMED CT
- Reference to two kinds of disorders (ontological types / concepts)
- Semantic relation between both
- **Epistemic** context: represents state of knowledge about a clinical situation
- Not clear whether there is really some heart failure at all!

- Many entries in EHRs must not be interpreted as factual statements
- Blending of ontological and epistemic information in one code characteristic for many clinical terminologies
"Suspected heart failure caused by ischaemic heart disease"

- Three heterogeneous representations of the same statement
- Three different atomic information entities
“Suspected heart failure caused by ischaemic heart disease”

**Annotation 1**

<table>
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</tbody>
</table>

- is a diagnosis about organ failure
- is a suspected organ failure diagnosis
- is a organ failure diagnosis about a disorder caused by ischaemic heart disease
“Suspected heart failure caused by ischaemic heart disease”

Annotation 1

- Diagnosis
  - is about only (OrganFailure)
  - has Locus some Heart

Organ Failure Diagnosis

- Organ: Heart
- Status: Suspected
- Caused by ischaemic heart disease: Yes

- Diagnosis is a suspected organ failure diagnosis
- Diagnosis is about a disorder caused by ischaemic heart disease
“Suspected heart failure caused by ischaemic heart disease”
Annotation 2

Diagnosis

Suspected heart failure caused by ischaemic heart disease

is a diagnosis

is a suspected diagnosis about heart failure caused by ischaemic heart disease

Diagnosis and isAbout only (HeartFailure and (causedBy some IschaemicHeartDisease)) and (hasQuality some Suspected)
“Suspected heart failure caused by ischaemic heart disease”

Annotation 3
One diagnosis instance for each model

<table>
<thead>
<tr>
<th>Organ Failure Diagnosis</th>
<th>Diagnosis</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organ</strong></td>
<td>Heart</td>
<td>Heart Failure</td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Suspected</td>
<td>Suspected</td>
</tr>
<tr>
<td><strong>Caused by ischaemic heart disease</strong></td>
<td>Yes</td>
<td>Ischaemic heart disease</td>
</tr>
</tbody>
</table>

- **Diagnosis_1**: Type Diagnosis and (isAbout only (Disorder and (causedBy some IschaemicHeartDisease)))
- **Diagnosis_2**: Type Diagnosis and (hasQuality some Suspected) and (isAbout only (HeartFailure and (causedBy some IschaemicHeartDisease)))
- **Diagnosis_3**: Type Diagnosis and (isAbout only HeartFailure)
Query 1

Query (class expression)

Diagnosis and isAbout only (HeartFailure and (causedBy some IschaemicHeartDisease)) and (hasQuality some Suspected)

Query results

Equivalent classes (1)

• Diagnosis_about_suspected_heart_failure_caused_by_ischaemic_heart_disease

Ancestor classes (11)

• Diagnosis
• Diagnosis_about_condition
• Diagnosis_about_disorder_caused_by_ischaemic_heart_disease
• Diagnosis_about_heart_disorder
• Diagnosis_about_heartfailure
• Diagnosis_about_heart_failure
• Diagnosis_about_heart_failure_caused_by_ischaemic_heart_disease
• Diagnosis_about_organ_failure
• Diagnosis_about_suspected_condition
• Diagnosis_about_suspected_organ_failure
• InformationArtefact
• Thing

Instances (3)

• Diagnosis_3
• Diagnosis_1
• Diagnosis_2

All three information instances found
Query 2

Query (class expression)

Diagnosis_about_heart_failure and
Diagnosis_about_suspected_condition and
Diagnosis_about_disorder_caused_by_ischaemic_heart_disease

Query results

Equivalent classes (1)

Diagnosis_about_suspected_heart_failure_caused_by_ischaemic_heart_disease

Instances (3)

Diagnosis_3

Diagnosis_1

Diagnosis_2

All three information instances found
Open issues (I)

- Accept semantic resources as they are (including what is considered “bad practice” by some), or more prescriptive approach (enforce distinction between terminology and information model)
- Is OWL appropriate to provide appropriate patterns to express “second-order” statements? Alternatives?
- Does the required expressivity (OWL DL + concrete domains) render the framework intractable?
- Query languages: DL, SPARQL, combinations?
- Semantic annotation of formal clinical guidelines?
Open issues (II)

- Is it realistic that IM developers will invest efforts into correctly use OWL for IM annotations?
- Education, training, modification of engineering and maintenance workflows?
- Will the ontological foundation of clinical terminologies be reliable and quality assured?
- To which extent semantic standards will be adopted at all?
- Possibility to use approach for semantic interpretation of text-mined content
Which are the main scenarios of use?

- Semantic abstraction for querying as demonstrated: using ontology based representation and querying (generic)
- Semantically-enriched data transfer: via semantic abstraction difficult. Rule-based approach (non-generic)?
Further readings
Ontology on the Web

- Description Logics: http://dl.kr.org/
- Protégé: http://protege.stanford.edu/
- Bioontology: http://www.bioontology.ch/
- Buffalo Ontology Site: http://ontology.buffalo.edu/smith/
- OBO Foundry: http://obofoundry.org/
- Bioportal: http://bioportal.bioontology.org/
- SNOMED CT: http://www.ihtsdo.org/snomed-ct/
  http://terminology.vetmed.vt.edu/sct/menu.cfm
- CO-ODE (Pizza ontology): http://www.co-ode.org/
- GoodOD Guideline: http://www.iph.uni-rostock.de/GoodOD-Guideline.1299.0.html
CLINICAL INFORMATION PATTERNS (WHAT, HOW)

- PAST HISTORY OF CONDITION / SITUATION:

  shn:InformationEntity and shn:isAboutSituation only (btl:BiologicalLife and btl:hasProcessualPart some shn:ClinicalSituation)

- PRIMARY DIAGNOSIS OF CONDITION / SITUATION:

  sct:HeartFailure

  shn:InformationEntity and shn:isAboutSituation only shn:ClinicalSituation and btl:outcomeOf some sct:DiagnosticProcedure

- SYMPTOM RECORD

  sct:SwollenAnkle

  shn:InformationEntity and shn:isAboutSituation only shn:ClinicalSituation and btl:outcomeOf some sct:EvaluationForSignsAndSymptoms
I. QUERY EXPRESSIVITY

Confirmed viral encephalitis diagnosis

The ability to support pre/post-coordination

FORM A:

<table>
<thead>
<tr>
<th>Diagnosis: A#1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease: Encephalitis</td>
</tr>
<tr>
<td>Cause: Virus</td>
</tr>
<tr>
<td>Status: Confirmed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Individual: Diagnosis_A Types A#1 and A#2 and A#3 and A#4</th>
</tr>
</thead>
<tbody>
<tr>
<td>45170000</td>
</tr>
</tbody>
</table>

FORM B:

<table>
<thead>
<tr>
<th>Main Diagnosis: B#1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease: Viral encephalitis</td>
</tr>
<tr>
<td>Status: Confirmed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Individual: Diagnosis_B Types B#1 and B#2 and B#3</th>
</tr>
</thead>
<tbody>
<tr>
<td>34476008</td>
</tr>
</tbody>
</table>

#QUERY: Give me all the patients with viral encephalitis diagnosed!!

>> Diagnosis_A
>> Diagnosis_B
II. SUBSUMPTION TESTING

Headache vs. Generalised headache

A specific condition means also a more general one

Form A

Symptoms: A#1
- Fever: Yes [x] No [ ] Unknown [ ]

A#2
- Headache: Yes [x] No [ ] Unknown [ ]

Form B

Signs and Symptoms: B#1
- Temperature value: 39 °C

B#2
- Headache: Yes [x] No [ ] Unknown [ ]

#QUERY: Give me all the patients that have headache symptom!!!

>> Symptom_Headache_A
>> Symptom_Headache_B
III. CONTEXT AWARENESS

Fever

Awareness of the **context**, independently of where it is represented (structure / terminology)

- **A#1**: `shn:Symptom` equivalentTo `shn:InformationItem` and `shn:isAboutSituation` only `shn:ClinicalSituation` and `btl:outcomeOf` some `sct:EvaluationSignsAndSymptoms`

- **A#2**: `shn:FeverSymptom` equivalentTo `shn:Symptom` and `shn:isAboutSituation` only `sct:FeverSituation`

- **B#1**: `shn:Symptom` equivalentTo `shn:InformationItem` and `shn:isAboutSituation` only `shn:ClinicalSituation` and `btl:outcomeOf` some `sct:EvaluationSignsAndSymptoms`

- **B#2**: `shn:SymptomTemperature39` `shn:ObservationResult` and `shn:isAboutQuality` only `(shn:Temperature` `btl:inheresIn` `some` `shn:corePartBody` and `btl:qualityLocated` only `shn:TemperatureValue` `value 39` and `btl:outcomeOf` some `sct:EvaluationSignsAndSymptoms` and `shn:hasObservableValue` value 39

**CGI axiom**

\[
\text{if (Temperature} > 37.2) \text{subClassOf} \text{shn:FeverSymptom}
\]

**#QUERY**: Give me all the patients that have fever symptom!!!

- `Symptom_Fever_A`
- `Symptom_Fever_B`