Implementing an Observables Ontology for SNOMED CT and LOINC Decision Support

James R. Campbell MD
W. Scott Campbell PhD
Jay Pedersen MS

Departments of Internal Medicine and Pathology
University of Nebraska Medical Center
Acknowledgements

- Allison Cushman-Vokoun MD PhD
- Geoffrey Talmon MD
- Audrey Lazenby MD
- Raj Dash MD
- Mary Kennedy
- Observable project team
- iPaLM SIG
Outline

- The role of Observable entities in interoperability
- Harmonized LOINC - SNOMED CT observables ontology
- Decision support use cases from QRDA reporting, genomic treatment selection and guidelines
- Observables ‘groupers’ for Epic decision support
- Observables ontology in i2b2 and Neo4j
ONC Terminology Model for Semantic Interoperability

- Demographics: LOINC, HL7/OMB code set
- Social and medical history: SNOMED CT
- Problem list/encounter diagnoses: SNOMED CT / ICD-10-CM
- Lab results (observables): Lab LOINC
- Physical findings: LOINC, SNOMED CT observables
- Medication orders: RxNORM, SNOMED CT
- Laboratory Orders: LOINC
- Immunizations: CVX, MVX
- Procedures: CPT, HCPCS
- Documents: LOINC
ONC Terminology Model for Semantic Interoperability: How it relates SNOMED CT and LOINC

- Demographics: (Clinical) Observables
- Social and medical history: Findings and Situations
- Problem list/encounter diagnoses: SNOMED CT / ICD-10-CM
- Lab results (observables): (Laboratory) Observables
- Physical findings: (Clinical) Observables
- Medication orders: RxNorm
- Laboratory Orders: (Laboratory) Orderables
- Immunizations: CVX, MVX
- Procedures: CPT, HCPCS
- Documents: LOINC
Introducing: Observable entity…What?

IHTSDO

“Observables are considered to be partial observation results, where there is a defined part of the observation missing.”

“Concepts in this hierarchy can be thought of as representing a question or procedure which can produce an answer or a result”

“Observable entity + Evaluation (test) result = Finding”

Regenstrief institute: LOINC

“…a set of universal names and ID codes for identifying laboratory and clinical test results”

“…master file of standard ‘test’ names and codes that will cover most of the entries in these files of operational laboratory systems”

“…organization of LOINC is divided first into four categories, ‘lab’, ‘clinical’, ‘attachments’ and ‘surveys’ ” (Lab and clinical are semantically equivalent to observables)
LOINC – SNOMED CT
Harmonization of Observable entities

- 2008 agreement between Regenstrief (RI) and IHTSDO
  https://loinc.org/collaboration/ihtsdo/agreement.pdf
  - Extend and harmonize a shared concept model for 363787002|Observable entity|
  - Map and instantiate LOINC parts in SNOMED CT content
  - Jointly publish expression data set defining (lab) LOINC concepts within the harmonized concept model
  - Technology preview alpha January 2016

- Assertion: What is needed to support clinical decision making and research with big data is a unified domain ontology for Observable entities spanning clinical and research content including genomics
Observables Project: Concept model draft
Step by step to create an Observables Ontology

- Implement SNOMED CT International release using SNOW OWL authoring platform
- Install Nebraska Lexicon© SNOMED CT extension; author new content needed for expanded SNOMED CT concept model
- Convert Observables technology preview to OWL format and install
- Import OWL axioms for gene and protein ontology from NCBI
- Run SNOMED CT and extensions through a description logic classifier
- VOILE!
Decision criteria which cannot be answered by aggregate query of LOINC or SNOMED CT

- Identify all diabetic patients with no hemoglobin A1C in the last 6 months
- Pull all cases records of colon cancer patients that have reports of tumor budding
- Find all patients who have tested positive for sickle related hemoglobinopathy
- Pull all historical cases for research of (colon) cancer with any gene biomarker testing completed
Decision queries which cannot be answered by query of LOINC or SNOMED CT

- Meaningful Use QA reporting: Identify all diabetic patients with no hemoglobin A1C in the last 6 months
- PathM: Pull all cases records of colon cancer patients that have reports of tumor budding
- LM: Find all patients who have tested positive for hemoglobin other than HbA
- PersM: Pull all historical cases of colon cancer with BRAF gene testing for research
Quality reporting criteria: Hemoglobin A1C values

- Common lab test assessing diabetic control; an outcome measure followed for quality of diabetic care
- RELMA code review: “Hemoglobin A1C”
- NLM valueset authority center: 17855-8, 17856-6, 4548-4, 4549-2
- Frequent confusion in proper code leads to miscoding in the clinical laboratory in the face of seven possibilities
Quality reporting criteria: Hemoglobin A1C values

- Common lab test assessing diabetic control; an outcome measure followed for quality of diabetic care
- RELMA code review: “Hemoglobin A1C”
- NLM valueset authority center: 17855-8, 17856-6, 4548-4, 4549-2
Find all hemoglobin A1C/Hgb measurements for patient

- Observable entity:
  - Component = 259690008|Glycosylated hgb-c fraction(substance)|
  - Direct site<<119297000|Blood specimen(specimen)|
  - Property type = 118542001|Mass fraction(property)|
  - Relative to = 38082009|Hemoglobin (substance)|
Find all hemoglobin A1C/Hgb measurements for patient

Observable entity:
Decision queries which cannot be answered by query of LOINC or SNOMED CT

- **MU**: Identify all diabetic patients with no glycated hemoglobin in the last 6 months
- **Clinical Pathology**: Pull all case records of colon cancer patients that have reports of tumor budding
- **LM**: Find all patients who have tested positive for hemoglobin other than HbA
- **PersM**: Pull all historical cases of colon cancer with BRAF gene testing for research
What is Tumor budding?

- A microscopic finding by the pathologist noting focal extension of tumor mass into surrounding tissue
- Not found in LOINC 2.54 or US Ed SNOMED CT 20160901
- Requested by one of our senior pathologists as part of a research protocol
- CAP Cancer synoptic standards treat this as an optional data element
Nebraska Lexicon for CAP Cancer checksheets

- 629949841000004100|Number of tumor buds per high power field observed in excised carcinoma (observable entity)|:
  - Inheres in: Malignant neoplasm
  - Direct site: Formalin-fixed paraffin embedded tissue specimen
  - Property type: Histologic invasiveness
  - Technique: Light microscopy
  - Towards: Tumor budding observed
Nebraska Lexicon for CAP Cancer checksheets

- 629949841000004100 | Number of tumor buds per high power field observed in excised carcinoma (observable entity):

  - Inheres in: Malignant neoplasm
  - Direct site: Formalin-fixed paraffin-embedded tissue specimen
  - Property type: Histologic invasiveness
  - Technique: Light microscopy
  - Towards: Tumor budding observed
## Terminology development summary: CAP Colorectal and Breast Cancer checksheets

<table>
<thead>
<tr>
<th>SNOMED CT hierarchy</th>
<th>Anatomic Pathology Concepts/Primitives</th>
<th>Molecular Genetic Concepts/Primitives</th>
<th>Exemplar molecular extension concepts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observable entities</td>
<td>61/1</td>
<td>32/3</td>
<td>“BRAF nucleotide sequence detected in excised malignancy”</td>
</tr>
<tr>
<td>Body Structures</td>
<td>10/9</td>
<td>29/3</td>
<td>“BRAF gene locus”</td>
</tr>
<tr>
<td>Clinical findings</td>
<td>6/2</td>
<td>7/3</td>
<td>“BRAF V600E variant identified in excised malignancy”</td>
</tr>
<tr>
<td>Procedures</td>
<td>2/1</td>
<td>0</td>
<td>“Pyrosequencing”</td>
</tr>
<tr>
<td>Techniques</td>
<td>4/4</td>
<td>7/7</td>
<td></td>
</tr>
<tr>
<td>Property types</td>
<td>8/8</td>
<td>2/2</td>
<td>“Sequence property”</td>
</tr>
<tr>
<td>Scale types</td>
<td>0</td>
<td>9/9</td>
<td>“Variant call format”</td>
</tr>
<tr>
<td>Situations</td>
<td>1/0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Substances</td>
<td>0/0</td>
<td>11/11</td>
<td>“BRAF human cellular protein”</td>
</tr>
<tr>
<td>Attributes</td>
<td>2/2</td>
<td>3/3</td>
<td></td>
</tr>
<tr>
<td>Qualifiers</td>
<td>2/2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>TOTALS</td>
<td>88/29</td>
<td>100/41</td>
<td></td>
</tr>
</tbody>
</table>
Decision queries which cannot be answered by query of LOINC or SNOMED CT

- MU: Identify all diabetic patients with no glycated hemoglobin in the last 6 months
- PathM: Pull all cases records of colon cancer patients that have reports of tumor budding
- Laboratory Medicine: Find all patients who have tested positive for sickle related hemoglobinopathy
- PersM: Pull all historical cases of colon cancer with BRAF gene testing for research
ACIP Guidelines for Pneumococcal Vaccination: Case of Hemoglobinopathy

- Special populations: Asplenia; Immunosuppressed; Sickle cell disease or Hemoglobinopathy; …
- NLM VSAC: SNOMED CT clinical findings
- Hemoglobinopathy:

  Computable Phenotypic criteria:
  - Problem list contains active problem $<<|\text{Hemoglobinopathy}\text{(disorder)}|$
  - Lab testing verifies abnormal hemoglobin?
ACIP Guidelines for Pneumococcal Vaccination: Case of Hemoglobinopathy

- Special populations: Asplenia; Immunosuppressed; Sickle cell disease or Hemoglobinopathy; ...

- NLM VSAC: SNOMED CT clinical findings

---

### NLM VSAC: SNOMED CT clinical findings

<table>
<thead>
<tr>
<th>Value Set Name</th>
<th>Sickle Cell Disease SNOMEDCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>OID</td>
<td>2.16.840.1.113762.1.4.1029.33</td>
</tr>
<tr>
<td>Type</td>
<td>Extensional</td>
</tr>
<tr>
<td>Definition Version</td>
<td>20160722</td>
</tr>
<tr>
<td>Steward</td>
<td>The Joint Commission</td>
</tr>
</tbody>
</table>

**This update was generated by VSAC to align with code changes published by SNOMEDCT**

<table>
<thead>
<tr>
<th>Expanded Code List</th>
</tr>
</thead>
<tbody>
<tr>
<td>Code</td>
</tr>
<tr>
<td>--------------------</td>
</tr>
<tr>
<td>127040003</td>
</tr>
<tr>
<td>127041004</td>
</tr>
<tr>
<td>127045008</td>
</tr>
<tr>
<td>127047000</td>
</tr>
<tr>
<td>127048005</td>
</tr>
<tr>
<td>23269001</td>
</tr>
<tr>
<td>25472008</td>
</tr>
<tr>
<td>35434009</td>
</tr>
<tr>
<td>35072007</td>
</tr>
<tr>
<td>35389006</td>
</tr>
<tr>
<td>416290001</td>
</tr>
<tr>
<td>416417002</td>
</tr>
<tr>
<td>416826005</td>
</tr>
</tbody>
</table>
Sickle cell hemoglobin measurements

- Observable entity:
  - Component: <<50095005 Hemoglobin S (substance)
  - Direct site = 119297000 Blood specimen(specimen)
  - Technique = 258035006 High pressure liquid chromatography(technique) OR 743050007 Electrophoresis(technique)
Decision queries which cannot be answered by query of LOINC or SNOMED CT

- **MU**: Identify all diabetic patients with no glycated hemoglobin in the last 6 months
- **PathM**: Pull all cases records of colon cancer patients that have reports of tumor budding
- **LM**: Find all patients who have tested positive for hemoglobin other than HbA
- **Personalized Medicine**: Pull all historical cases of colon cancer for research which had any tumor biomarker testing
Molecular genetics testing of neoplasms

- Rapidly expanding field of research with nucleotide and chromosomal findings showing value for diagnosis, prognosis and treatment planning
- Large body of work in molecular genetics continuing to grow
- Expanded content model for Observables has SNOMED CT content to include genes and proteins defined by reference to NCBI scientific databases
Tumor biomarker Observable

455350031000004100|BRAF nucleotide sequence detected in excised malignant neoplasm(observable entity)

363787002|Observable entity|

923178251000004106|Sequence variant property|

367651003|Malignant neoplasm (morphology)|

100670521000004106|BRAF gene locus (cell structure)|

123029007|Single point in time|

59816316100000410|Variant call format|

59816316100000410|Nucleotide sequencing technique|

441652008|Formalin fixed paraffin embedded tissue specimen|
Cancer case with tumor biomarkers accomplished

- Observable:
  - Inherent location: <<< 367651003 Malignant neoplasm(morphology)
  - Inheres in: <<< 590638411000004104 Nucleotide sequence(cell structure)
  - Technique: <<< 708068002 Molecular genetics(technique)
Cancer case with tumor biomarkers accomplished

- Observable:
  - Inherent location: << 367651003 Malignant neoplasm (morphology)
  - Inheres in: << 590638411000004104
Observables Ontology Applications

- Clinical decision support in Epic; creation of observables Groupers
- Indexing cancer biorepository using SNOMED CT and graph database
- Implementation of Observables ontology as i2b2 metadata
Observables Ontology

Applications

- Clinical decision support in Epic; creation of observables Groupers
- Indexing cancer biorepository using SNOMED CT and graph database
- Implementation of Observables ontology as i2b2 metadata
Questions?