Applications of OBI 'assay'

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***Abstract*—We discuss the applicability of using the OBI assay paradigm for representing patient questionnaires, neuropsychological tests, and neurological exams, as well to annotate data generated from these assessments. We conclude that the specification for OBI 'assay' employs a broad enough notion of evaluation to allow for these uses. However, it would be preferable to introduce subclasses of OBI 'planned process' or OBI 'assay' that explicitly addresses these types of use cases and provides clear groupings for general types of assays.**

Keywords—assay; OBI; questionnaire; neuropsychological test; neurological exam; clinical history

I. BACKGROUND

The Ontology for Biomedical Investigations (OBI) is an integrated ontology for the description of biological and clinical investigations [1]. OBI is a domain ontology that provides a set of terms and relations to support precise annotation and querying of the data generated in biomedical investigations. It represents the design, types of analyses and assays performed, specifications, and data generated, resulting in classes such as 'assay', 'plan specification', and 'measurement datum'. OBI defines 'assay' as "a planned process with the objective to produce information about the material entity that is the evaluant, by physically examining it or its proxies" [2]. All assays have a specified output, an information content entity, which is about the evaluant. Examples of usage are: "Assay the wavelength of light emitted by excited Neon atoms. Count of geese flying over a house." Subclasses of OBI 'assay' include many laboratory-specific examples, such as 'sequencing assay' and 'metabolite profiling'. However, other types include 'performing a clinical assessment', 'age measurement assay', and 'handedness assay'.

Several projects are underway which seek to represent and annotate data generated from different types of forms, questionnaires, and tests. Each of these uses-cases broaden the application of OBI 'assay' in one or more ways.

Neuropsychological tests are used to assess cognitive domains such as attention, visual-spatial ability, memory, executive function, and language comprehension and expression. In addition to representing the structure of these neuropsychological tests, it is crucial to capture the cognitive processes and functions that they evaluate as well as the data they produce. The neuropsychological Testing Ontology (NPT) utilizes OBI's assay paradigm to represent these tests [3]. The handedness assay was used as a starting point to model these tests. However, difficulties have been encountered in relating the assay process to the cognitive processes and functions being evaluated. Also, cognitive functions, such as short-term memory, cannot be the bearer of measureable qualities. The solution in NPT is to connect a cognitive process to the function it realizes in the assay process using a new relationship between a data item and a function.

The Multiple Sclerosis Patient Data Ontology (MSPD) has been developed to represent both clinical measures and patient reported outcomes (PRO) associated with the New York State Multiple Sclerosis Consortium (NYSMSC) patient data registry [4]. A PRO is generally considered to be an assessment of any aspect of a patient's health status that comes directly from the patient and without any interpretation by a clinician [5]. The data registry uses standardized forms addressing demographic and clinical information, disease status and progression. It also includes data pertaining to patients' perception of their quality of life and wellbeing, which includes assessment of physical and psychosocial impairment. During the enrollment process patients are asked to rate their perception of their own functional abilities and affective states. A difficulty in using the assay framework has been in reconciling what qualifies as a physical examination and subsequent evaluation. An output of a survey in which a patient is asked to make a judgment about his or her perceived limitation in a particular limb or visual acuity may indeed qualify in this case as a sort of post-hoc physical exam which allows the evaluant to also be the evaluator. The OBI 'self-reported handedness assessment' supports the application of 'assay' to cases where a patient self-evaluates outside the context of a direct physical exam.

However, it is less clear how questionnaires and forms that obtain basic demographic data fit within OBI's account of assays. A patient responding to questions such as date of birth, marital status, insurance provider, etc. pushes one to reconsider what is being evaluated, especially since no physical examination is involved.

A related project is the development of an ontology-based medical history module to extend a legacy clinical information management system. This module collects, structures, and stores data using OBO Foundry ontologies and semantic web technology. Part of this work involves the development of an ontological model for health history questionnaires, each consisting of a series of questions to be answered by the patient during a medical history interview session. While many question answers that make up a patient's clinical history are clearly about the patient's body or are the result of some physical examination of the patient, others do not seem to fit the OBI assay framework. Family history questions are

problematic in this regard. So are questions about the existence of a previous diagnosis, such as "Has a doctor ever told you that you had a myocardial infarction or heart attack?" [6]. The planned process of soliciting an answer to this question is intended to produce information about physical entities (the patient; her heart) as well as information about related entities such as diagnoses. However, asking and answering this question and recording the answer does not directly involve a physical examination. An answer of "yes" to this question most likely indicates that a previous assay resulted in the original diagnosis; however it is much more difficult to argue for any connection between an answer of "No" (or "I'm not sure") and any sort of physical examination.

II. Conclusion

As it is currently defined, OBI 'assay' allows for a broad interpretation of what it means to physically examine or evaluate a patient. While neuropsychological tests and clinical exams can be made to fit within the assay framework, modification is required. Subjects being asked to evaluate aspects of their own bodily functioning or cognitive and affective status provides another challenge for understanding and implementing OBI 'assay', yet this ontological class can still provide a plausible solution. However, questionnaires, demographic information, and factual tests with no interpretive or summary outputs go beyond what can be accomplished using OBI 'assay'. As a result, they raise interesting questions about what modifications or additions to OBI are required.

Our poster details the discussed uses of OBI 'assay' and summarizes the difficulties encountered. We offer alternatives and suggest the inclusion of a general set of assay and planned process types which will aid in recognizing distinctions between the various assessment strategies. Our hope is that this work will promote development in OBI and assist others who are using the assay paradigm in OBI.

References

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[6] https://www.phenxtoolkit.org/index.php?pageLink=browse.protocoldetails&id=40801

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Introduction

The Ontology for Biomedical Investigations (OBI) is an integrated ontology for the description of biological and clinical investigations. It represents the design, types of analyses and assays performed, specifications, and data generated during an investigation. Thus, it provides classes such as 'assay', 'plan specification', and 'measurement datum'. An assay is a planned process which produces information about an evaluant. Examples of assays include: "assay the wavelength of light emitted by excited neon atoms" and "count the number of geese flying over a house." Subclasses of OBI 'assay' include laboratory-specific examples, such as 'sequencing assay' and 'metabolite profiling'. However, other types include 'performing a clinical assessment', 'age measurement assay', and 'handedness assay'. Several projects at the University at Buffalo seek to represent and annotate data generated from different types of questionnaires, forms, and tests. Each of these provide a use case that broadens the current application of OBI 'assay' in one or more ways, possibly stretching its applicability.

OBI Assay

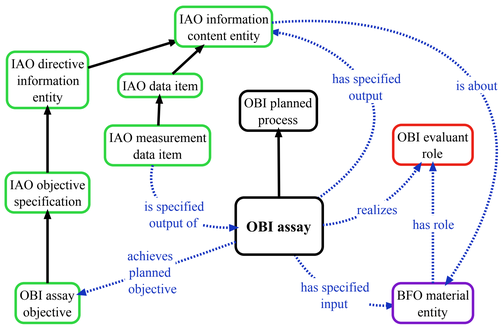
The class 'assay' is central to OBI's purpose and utility. The paradigm for representing assays involves several key components that relate to the assay class, as shown below. The evaluant role specifies the mode of participation in the assay for the entity under study. The measurement data item represents information derived from executing an assay. The assay objective specifies the goal of the assay. Each of these is essential to representing and differentiating subtypes of assay.

OBI assay is a planned process with the objective to produce information about the material entity that is the evaluant, by physically examining it or its proxies.
Equivalent to: (achieves_planned_objective some 'assay objective').

OBI assay objective is an objective specification to determine a specified type of information about an evaluated entity (the material entity bearing evaluant role).

OBI evaluant role is a role that inheres in a material entity that is realized in an assay in which data is generated about the bearer of the evaluant role.
Subclass of: ('is realized by' only assay).

I**AO measurement data item** is a data item that is a recording of the output of an assay.



Black are processes, **green** are information content entities, **purple** are material entities, and **red** are realizable entities.

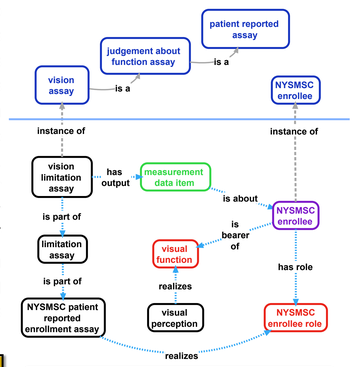
Example of Canonical Use Case

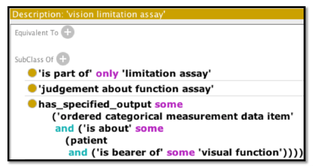
OBI 'assay' has many subclasses. Among these, the 'analyte assay' classes represents "classic" laboratory assays in which a substance with an analyte role is detected in a mixture, which bears the evaluant role. Other OBI assays omit naming of the analyte and its role, but follow a similar design pattern, where the evaluant role is reserved for the entity under study.

A key question is whether the material entity bearing the evaluant role can be a sentient creature, a person, who may be assayed via observation or direct questioning to yield information that is about non-material aspects of that person. A precedent for this in OBI is the 'handedness assay' and its subclasses, which represent assays about the handedness of a person.

Multiple Sclerosis Patient Data Ontology (MSPD)

MSPD has been created to represent clinical measures and patient reported outcomes obtained from enrollment forms used by centers participating in the New York State Multiple Sclerosis Consortium. Enrollees asked to rate, for example, aspects of their bodily functioning, the extent of their pain, or life satisfaction could be said to be producing information about themselves as the evaluant.

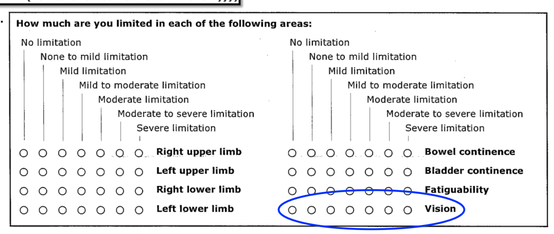




Above is an example of MSPDs application of OBI 'assay'. Boxes below the blue line are instances of classes named inside the box.

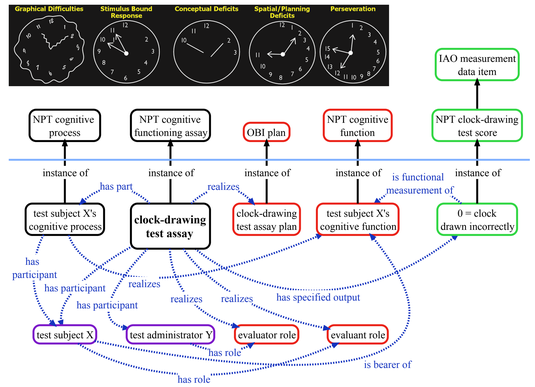
Left is a example of an axiom in the vision limitation assay.

Below is a portion of the patient reported component of the enrollment form.



NeuroPsychological Testing Ontology (NPT)

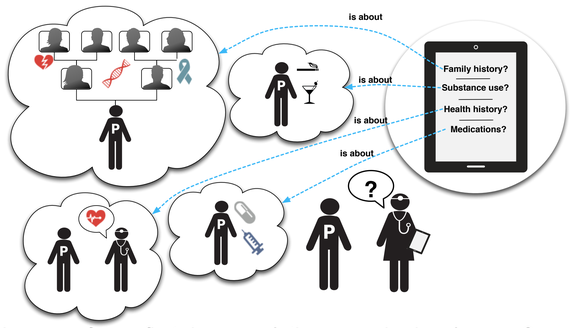
Neuropsychological tests are used to assess cognitive domains such as attention, visual-spatial ability, memory, executive function, and language. NPT uses the assay paradigm to represent these tests. The OBI 'handedness assay' was used as a starting point to model neuropsychological tests. However, difficulties arose when relating the results of neuropsychological assays to cognitive processes and functions. In particular, a cognitive function – such as short-term memory or executive function – cannot be the bearer of a quality. To resolve this issue, we created a new relationship, 'is functional measurement of', to connect neuropsychological test results to the cognitive functions being evaluated.



Above is a partial representation of the Clock-Drawing Test in NPT. Above that are examples of common mistakes made by test participants.

Medical History Collection

One of our projects is an ontology-based medical history module that is part of a larger clinical information management system. It stores structured representations of questions and answers about patients' medical histories. The process of completing a medical history questionnaire has as its parts assay-like planned processes to produce information about the patient, but many do not involve *physically* examining the patient or anything else. Example questions derived from the PhenX Toolkit [1] appear below.



- Has any of your first degree relatives ever had melanoma?
- Has a doctor or nurse ever said that you have high blood pressure or hypertension?
- Have you smoked at least 100 cigarettes in your entire life?
- In the past 3 years, please indicate if you have taken either of the following types of medications:
  Statin medications such as lovastatin, …

[1] https://www.phenxtoolkit.org/

Problems Encountered in Applications of OBI 'assay'

- OBI lacks diversity in the types of assays represented. While the original scope of 'assay' seems grounded in prototypically "wet" laboratory assays, its definition does not restrict its application to these cases.
- Elucidation for the concepts of evaluation and measurement is needed. If possible, formal definitions should be provided.
- The exact relationship between assays and their outputs is unclear. All measurement data items have to be the output of some assay, but not all assays have to output a measurement data item. Thus, assays can have outputs that are not measurement data items. Furthermore, all assay output data must be about a material entity that bears an evaluant role. This complicates the representation of assays designed to evaluate non-material entities.
- It is not clear how filling out questionnaires or forms that obtain basic demographic data fit within OBI's account of assay. A patient responding to questions such as date of birth, marital status, insurance provider, etc. pushes one to reconsider what is being evaluated—especially since no physical examination is involved. Can a patient evaluate oneself? Also, does an ordinal ranking of pain count as a measurement?

Solutions

- Examples of non-assay planned processes that produce information about evaluants should be provided to illuminate the distinction between these classes.
- Develop paradigmatic assay applications and make current applications consistent in their representation.
- Objective specification should be specified to relate to the evaluation in the assay, not just the type of information.
- Providing general subtypes of assay to group its current subtypes would help address these shortcomings. For example, assays could be grouped by the nature of their evaluants, the type of evaluation process, or their objectives. Membership in these groupings could be inferred by enforcing the use of consistent logical definitions for assay subtypes.

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