



Semantic Representation of Evidence-Based Medical Guidelines and Its Use Cases

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Abstract: Semantic representation of evidence-based medical guidelines provides the support for the data inter-operability and has been found many applications in the medical domain. In this paper, we describe a semantic representation approach of evidence-based medical guidelines, which is based on the Semantic Web Technology standards. We discuss several use cases of that semantic representation of evidence-based medical guideline, and show that they are potentially useful for medical applications.

Key words: evidence-based medical guidelines; semantic representation; semantic technology; use cases

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0 Introduction

Evidence-based medical (EBM) guidelines are important knowledge resources which have been used in many medical decision support systems and medical applications. Clinical guidelines are concrete recommendations on the appropriate treatment and care of people with specific diseases and conditions from the clinical perspective. Thus, clinical guidelines can be considered to be a special kind of medical guidelines. Clinical guidelines have been proved to be very valuable for clinicians, nurses, and other health-care professionals in their work.

Existing Evidence-based medical guidelines are usually in the textual format. This textual format has following limitations:

① Textual guideline information cannot be shared, searched and extended easily.

② Textual guideline information cannot be understood by computers, which results in key obstacles for automatic guideline update.

Although there exist several formalisms for computerized clinical guidelines, called computer-interpretable guidelines (CIGs), like those in PROforma^[1,2], Asbru^[3], EON^[4], GLIF^[5,6], which implement the guidelines in computer-based decision support systems, those existing formalisms of clinical guidelines require heavy manual labor for the generalization. A semantic representation of evidence-based medical guidelines has been proposed in our previous paper^[7]. In that approach, evidence-based guidelines are represented by using the Semantic Web

technology standards such as RDF/RDFS/OWL standards. This light weighted formalism of evidence-based medical guidelines has the advantage that they can be generated quite easily by using the NLP tool and the Semantic Web technology. In this paper, we provide a detailed discussion on that semantic representation approach. Furthermore, we discuss the use cases of that approach as an extension to our previous work, which include the following work:

① Correctness checking of evidence-based medical guidelines. Due to the manual processing and generalization of medical guidelines, many existing medical guidelines may contain various errors or inconsistencies. The formalization of medical guidelines provide the possibility for us to check the correctness of their representations. We will show how to use semantic queries (e.g. SPARQL queries) to detect errors in evidences-based medical guidelines.

② Finding new medical evidences for guideline update. New medical research publications are rapidly growing and these publications may offer new evidences for supporting the update of the Evidence-Based Medical Guidelines. The traditional way of new relevant evidence finding for the EBM guideline update is done by manual retrieval and analysis, which is time-consuming and often cannot track the latest research relevant evidences. Automatically finding relevant evidences by computers has been considered to improve the efficiency of guideline update. We will show how to find evidences for evidence-based medical guidelines.

This paper is organized as follows: Section 1 describes the idea of semantic representation of evidence-based medical guidelines. Section 2 presents the detail application use cases based on the semantic presentation format of EBM guidelines and shows their results, respectively. Section 3 makes the conclusions.

1 Semantic Representation of EBM Guidelines

1.1 The Structure of EBM Guidelines

Evidence-based medical guidelines are a series of conclusions on clinical care, supported by the best available evidences. In EBM guidelines, the most important knowledge is the conclusions. Those conclusions in the guidelines are the main knowledge we focus on. Every conclusion in EBM guideline consists of the following four parts:

① Evidence level of conclusions, which states how strong the conclusion is supported by its evidences;

② Statement of the conclusion, alternatively called Text of the conclusion, which contains the content of the conclusion;

③ Evidence class, which states which class the evidence has, according to their evidence classification;

④ Evidences, namely the references or the publications which support for the conclusion;

Here is an example of a typical conclusion, which is extracted from Dutch Breast Cancer Guideline 2012 version 2.0^[8]:

Level 2

The difference in accuracy between MRI and mammography is dependent on the density of the breast tissue. The difference is small for fatty breasts.

A2 Berg 2004, Sardanelli 2004,

B Van Goethem 2004, Schnall 2005

In the example above, the “Level 2” is the evidence level of the conclusion. The text “The difference in accuracy between MRI and mammography is dependent on the density of the breast tissue. The difference is small for fatty breasts” is the statement of the conclusion. The “A2” and “B” are the evidence classes. “Berg 2004, Sardanelli 2004, Van Goethem 2004 and Schnall 2005” are the detail evidences. Every conclusion in EBM guideline has the same structure.

Evidences in EBM guidelines are mainly obtained from the published scientific articles. The articles selected were evaluated by experts using some methodology for their research quality. In NABON^[8] and NSRS^[9], a classification of evidences (e.g. research results) are proposed, which consists of the following five classes: ① A1: Systematic reviews (i.e. research on the effects of diagnostics on clinical outcomes in a prospectively monitored, well-defined patient group), or that comprises at least several A2 quality trials whose results are consistent; ② A2: High-quality randomized comparative clinical trials (randomized, double-blind controlled trials) of sufficient size and consistency; ③ B: Randomized clinical trials of moderate quality or insufficient size, or other comparative trials (non-randomized, comparative cohort study, patient control study); ④ C: Non-comparative trials, and ⑤ D: Opinions of experts, such as project group members.

Based on the medical articles, one or more relevant conclusions are made for each section (i.e. each topic in the guidelines). The most important articles is listed according to the level of evidential strength, allowing con-

clusions to be drawn based on the level of evidence. There are four kinds of evidence level based on articles analysis: i) Level 1: based on one systematic review (A1) or at least two independent A2 reviews; ii) Level 2: based on at least two independent B reviews; iii) Level 3: based on one A2 or one B research, or any C research, and iv) Level 4: opinions of experts.

1.2 A Method of Formalizing EBM Guidelines in Semantic Technology

In this section, we briefly introduce our method of

```
sctid:gl003-qh141029 rdf:typesct:EvidenceBasedGuidelines.
sctid:gl003-qh141029 dc:title "Dutch Breast Cancer Guideline 2004".
sctid:gl003-qh141029 dc:creator "NABON".
sctid:gl003-qh141029 sct:publicationYear "2004".
sctid:gl003-qh141029 sct:hasGuidelineID "gl003".
sctid:gl003-qh141029>sct:hasConclusions sctid:gl003-qh141029_1.
sctid:gl003-qh141029_1 rdf:typesct:GuidelineConclusions.
sctid:gl003-qh141029_1 sct:about "Treatment of DCIS".
sctid:gl003-qh141029_1 sct:hasGuidelineItem sctid:gl003-qh141029_1_1.
sctid:gl003-qh141029_1_1 sct:hasText "Addition of radiotherapy following localexcision of DCIS results in a significantly lower risk of local recurrence(this is valid for all subgroups)." .
sctid:gl003-qh141029_1_1 sct:evidenceLevel "1"^^xsd:decimal.
sctid:gl003-qh141029_1_1 sct:hasReferences sctid:gl003-qh141029_1_1ref.
sctid:gl003-qh141029_1_1ref sct:hasReference sctid:gl003-qh141029_1_1ref1.
sctid:gl003-qh141029_1_1ref1sct:referencesctid:#gl003-zshref-Fish1998a .
sctid:gl003-qh141029_1_1ref1 sct:evidenceClassification "A2" .
sctid:gl003-qh141029_1_1ref1 sct:hasReference sctid:gl003-qh141029_1_1ref2.
sctid:gl003-qh141029_1_1ref2 sct:reference sctid:gl003-zshref-Fish1998b.
sctid:gl003-qh141029_1_1ref2 sct:evidenceClassification "A2" .
```

The statement above describes the guideline heading and the guideline item with their evidence levels and references.

The NLP tool that we use for the concept identification for the semantic annotations and the relation extraction is XMedlan and the Xerox linguistic-based module, which is developed for the European 7th Framework Project EURECA^[10].

The main characteristics of this component is that it

representing the EBM guidelines in semantic technology^[7]. The semantic representation of EBM guidelines consists of the following sections: ① Heading. The heading section of the guidelines provide the basic description of the information such as the title and provenance; ② Body. The body section provides the main description of guidelines and their evidences. It consists of a list of guideline items containing the evidence information and their semantic representations of a single guideline statement.

uses a linguistic parser^[11] to perform rich linguistic analysis of the input text. All the annotations produced by the linguistic analyzer are exploited by the relation extraction engine to identify relations and attributes of concepts and entities in the input text. These relations and attributes are expressed as triples, i.e. typed binary relations in the form of {Subject, Property, Object}.

Here is an example of serialized statements in the RDF NTriple format:

```
sctid:gl003-qh141029_1_1e1 ctec:isA sct:diagnosis.
sctid:gl003-qh141029_1_1e1 ctec:hasObject sctid:gl003-qh141029_1_1e2.
sctid:gl003-qh141029_1_1e2 ctec:hasTerm "recurrence".
sctid:gl003-qh141029_1_1e2 ctec:hasCUI "C0034897|C1458156".
sctid:gl003-qh141029_1_1e2 ctec:hasCodeSNOMEDCT "246455001".
sctid:gl003-qh141029_1_1e2 ctec:isAsct:disease_or_syndrome.
sctid:gl003-qh141029_1_1e3 ctec:isA sct:diagnosis.
sctid:gl003-qh141029_1_1e3 ctec:hasObject sctid:gl003-qh141029_1_1e4.
sctid:gl003-qh141029_1_1e4 ctec:hasTerm "DCIS".
sctid:gl003-qh141029_1_1e4 ctec:hasCUI "C0007124".
```

sctid:gl003-qh141029_1_1e4 ctec:hasCodeSNOMEDCT “86616005|278053004|189338004|109889007|189705006”.
sctid:gl003-qh141029_1_1e4 ctec:isAsct:disease_or_syndrome.
sctid:gl003-qh141029_1_1e5 ctec:isAsct:treatment.
sctid:gl003-qh141029_1_1e5 ctec:hasTerm “radiotherapy”.
sctid:gl003-qh141029_1_1e5ctec:hasCUI “C0243005|C1522449”.
sctid:gl003-qh141029_1_1e5ctec:hasCodeSNOMEDCT “419815003|108290001|302505005|61757002|182666000|150903009”.
sctid:gl003-qh141029_1_1e6 ctec:isAsct:treatment.
sctid:gl003-qh141029_1_1e6 ctec:hasTerm “local excision”.
sctid:gl003-qh141029_1_1e6 ctec:hasCUI “C0278259”.
sctid:gl003-qh141029_1_1e6 ctec:hasCodeSNOMEDCT “86743009”.
sctid:gl003-qh141029_1_1e5 ctec:hasObject sctid:gl003-qh141029_1_1e4.
sctid:gl003-qh141029_1_1e7 ctec:isAsct:EC.
sctid:gl003-qh141029_1_1e7 ctec:includes sctid:gl003-qh141029_1_1e6.
sctid:gl003-qh141029_1_1e7 ctec:hasText “addition of radiotherapy following localexcision of DCIS results in a significantly lower risk of local recurrence(this is valid for all subgroups).”.
sctid:gl003-qh141029_1_1 sct:hasRelations sctid:gl003-qh141029_1_1e7.
sctid:gl003-qh141029_1_1e7 ctec:hasFragment sctid:gl003-qh141029_1_1e1.
sctid:gl003-qh141029_1_1e7 ctec:hasFragment sctid:gl003-qh141029_1_1e3.
sctid:gl003-qh141029_1_1e7 ctec:hasFragment sctid:gl003-qh141029_1_1e5.
sctid:gl003-qh141029_1_1e7 ctec:hasFragment sctid:gl003-qh141029_1_1e8.
sctid:gl003-qh141029_1_1e8 ctec:hasTerm “valid”.
sctid:gl003-qh141029_1_1e8 ctec:hasCUI “C3275230”.
sctid:gl003-qh141029_1_1e7 ctec:hasFragment sctid:gl003-qh141029_1_1e9.
sctid:gl003-qh141029_1_1e9 ctec:hasTerm “results”.
sctid:gl003-qh141029_1_1e9 ctec:hasCUI “C2825142”.
sctid:gl003-qh141029_1_1 sct:hasGuidelineItemID “gl003-qh141029_1_1”.

The serialized statements in the RDF NTriple format states the guideline statement and the relation extractions from the statement. They provide the detail RDF description of the guideline statement and its annotation with the concepts in UMLS, a well-

known meta-thesaurus of medical terms developed^[12].

We also use the XMedlan NLP tool to make the annotation statement of the guideline conclusion with the SNOMED concepts, like this:

sctid:gl003-qh141029_1_1 ctec:hasAnnotation sctid:gl003-qh141029_1_1a1 .
sctid:gl003-qh141029_1_1a1 ctec:hasTerm “radiotherapy”.
sctid:gl003-qh141029_1_1a1 ctec:hasSenses sctid:gl003-qh141029_1_1a1s .
sctid:gl003-qh141029_1_1a1s ctec:Sense “419815003”.
sctid:gl003-qh141029_1_1a1s ctec:Source “SNOMEDCT_US”.
sctid:gl003-qh141029_1_1a1s ctec:Sense “108290001|302505005|61757002|182666000|150903009”.
sctid:gl003-qh141029_1_1a1s ctec:Source “SNOMEDCT_US”.
sctid:gl003-qh141029_1_1 ctec:hasAnnotation sctid:gl003-qh141029_1_1a2 .
sctid:gl003-qh141029_1_1a2 ctec:hasTerm “local excision”.
sctid:gl003-qh141029_1_1a2 ctec:hasSenses sctid:gl003-qh141029_1_1a2s .
sctid:gl003-qh141029_1_1a2s ctec:Sense “86743009”.
sctid:gl003-qh141029_1_1a2s ctec:Source “SNOMEDCT_US”.
sctid:gl003-qh141029_1_1 ctec:hasAnnotation sctid:gl003-qh141029_1_1a3 .
sctid:gl003-qh141029_1_1a3 ctec:hasTerm “DCIS”.
sctid:gl003-qh141029_1_1a3 ctec:hasSenses sctid:gl003-qh141029_1_1a3s .

sctid:gl003-qh141029_1_1a3s ctec:Sense "86616005|278053004|189338004|109889007|189705006".
sctid:gl003-qh141029_1_1a3s ctec:Source "SNOMEDCT_US".
sctid:gl003-qh141029_1_1 ctec:hasAnnotation sctid:gl003-qh141029_1_1a4.
sctid:gl003-qh141029_1_1a4 ctec:hasTerm "recurrence".
sctid:gl003-qh141029_1_1a4 ctec:hasSenses sctid:gl003-qh141029_1_1a4s.
sctid:gl003-qh141029_1_1a4s ctec:Sense "246455001".
sctid:gl003-qh141029_1_1a4s ctec:Source "SNOMEDCT_US".
sctid:gl003-qh141029_1_1a4s ctec:Sense "null".
sctid:gl003-qh141029_1_1a4s ctec:Source "SNOMEDCT_US".
sctid:gl003-qh141029_1_1 ctec:hasAnnotation sctid:gl003-qh141029_1_1a5.
sctid:gl003-qh141029_1_1a5 ctec:hasTerm "results".
sctid:gl003-qh141029_1_1a5 ctec:hasSenses sctid:gl003-qh141029_1_1a5s.
sctid:gl003-qh141029_1_1a5s ctec:Sense "null".
sctid:gl003-qh141029_1_1a5s ctec:Source "SNOMEDCT_US".
sctid:gl003-qh141029_1_1 ctec:hasAnnotation sctid:gl003-qh141029_1_1a6.
sctid:gl003-qh141029_1_1a6 ctec:hasTerm "local".
sctid:gl003-qh141029_1_1a6 ctec:hasSenses sctid:gl003-qh141029_1_1a6s.
sctid:gl003-qh141029_1_1a6s ctec:Sense "28468008|255470001".
sctid:gl003-qh141029_1_1a6s ctec:Source "SNOMEDCT_US".
sctid:gl003-qh141029_1_1a6s ctec:Sense "null".
sctid:gl003-qh141029_1_1a6s ctec:Source "SNOMEDCT_US".
sctid:gl003-qh141029_1_1 ctec:hasAnnotation sctid:gl003-qh141029_1_1a7.
sctid:gl003-qh141029_1_1a7 ctec:hasTerm "valid".
sctid:gl003-qh141029_1_1a7 ctec:hasSenses sctid:gl003-qh141029_1_1a7s.
sctid:gl003-qh141029_1_1a7s ctec:Sense "null".
sctid:gl003-qh141029_1_1a7s ctec:Source "SNOMEDCT_US".

It is interesting to see that the concept identification with systematized nomenclature of medicine (SNOMED) can identify more concepts than those detected by the relation extraction with UMLS by using the NLP tool. For example, the concept identification with SNOMED can find the concept "DCIS", which is not detected by the relation extraction with the UMLS concept identification.

2 Detailed Use Cases

After we obtain the semantic representation format of EBM guidelines, we try to do some detail application research using this kind of EBM guideline as the basic knowledge. The first use case is the correctness checking for the original EBM guideline. The second use case is the guideline update. This section describes the methods and the results of the two use cases.

2.1 Use Case I: Correctness Checking of EBM Guidelines

Due to the manual processing and generalization of medical guidelines, many existing medical guidelines

may contain various errors or inconsistencies. The formalization of medical guidelines provides the possibility for us to check the correctness of their representation. We will show how to use the semantic queries (e.g. SPARQL queries) to detect several errors in evidences-based medical guidelines. In the following, we discuss the method and results.

Based on the semantic representation format of EBM guideline, we can use SPARQL queries to do reasoning. In the correctness checking of EBM guideline, we mainly check whether the evidence levels of the conclusion meet their corresponding definitions.

Here is an example to detect the evidence level errors in the Dutch Breast Cancer 2012, version 2.0. For example, according to the definitions of the evidence level 1, which have been discussed in Section 1, if a conclusion is supported by at least two independent level B evidences, it must be the Level 2 conclusion. We can use the following SPARQL query to detect if there exists any guideline conclusion which is assigned to non-Level 2 with two independent level B evidences.

PREFIX xsd: <<http://www.w3.org/2001/XMLSchema#>>
PREFIX sct: <<http://wasp.cs.vu.nl/sct/sct#>>

```

PREFIX dc: <http://purl.org/dc/1.1#>
PREFIX rdf:
<http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX dbpedia3: <http://dbpedia.org/property/>
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX rdfs:
  <http://www.w3.org/2000/01/rdf-schema#>
select distinct ?id ?conclusionItem ?level
where{
?id0 sct:about ?topic.
?id0 sct:hasGuidelineItem ?id.
?id sct:hasText ?conclusionItem.
?id sct:evidenceLevel ?level.
?id sct:hasReferences ?id1.
?id1 sct:hasReference ?id2.
?id2 sct:evidenceClassification "B".
?id1 sct:hasReference ?id3.
?id3 sct:evidenceClassification "B".
FILTER (!(?id2=?id3)).
FILTER (!(?level=2)).
}

```

order by ?id

In the SPARQL query above, we use “FILTER (!(?level = 2))” to find non-level-two conclusions. The system can find that there exist two conclusions (gl002-zsh140412_12_3 and gl002-zsh140412_38_1), which are supported by at least two B reviews, but classified into ones with Level 3.

Namely, the following guideline items contain the error in the guidelines:

Level 3

If a corresponding laesion on ultrasound is not found, the chance of malignancy is 6.3% - 20%.

B La Trenta 2003, Sim 2005, Linda 2008, Demartini 2009, Meissnitzer 2009,

Destounis 2009, Abe 2010

We can also detect some evidences which have marked as a non-standard class. Table 1 shows the errors we have detected from the Dutch Breast Cancer Guideline 2012, Version 2.0^[8], errors means the inconsistency between the original evidence level of conclusions in the guidelines and the definitions.

Table 1 The detected errors from Dutch Breast Cancer Guideline2012, Version 2.0

Classification	Evidence level	Errors	Total	Ritio/%
Level 1	One A1 or Two independent A2	0	95	0.00
Level 2	Two independent B	6	46	13.04
Level 3	One A2 or One B or C	3	88	3.41
Level 4	Opinionsof experts	0	1	0.00

2.2 Use Case II: Guideline Update

Except the application in correctness checking of EBM guidelines, we also use the semantic representation formatted EBM guidelines in automatically finding new evidences for the guideline update.

In EBM guidelines, the evidences are based on published scientific research articles. Those articles are usually found in medical publications such as those in PubMed. An ideally evidence-based guideline should be updated immediately after new relevant evidence is published, but the reality is that the publications are growing very fast. For example, about 4 000 completed references are added in MEADLINE each day(MEADLINE is the most popular medical publication database). But the guideline update is very slow, from the beginning of guideline update to the publication of updated guideline, averagely it takes about 2 years, maybe the updated guideline is out of time after the guideline is publicized. Therefore, we must find a method to monitor the relevant latest articles to update the corresponding guideline in

time. In the following, we discuss the method and results.

The semantic representation of evidence-based medical guideline provides a foundation for these automatic finding evidences of medical guidelines for guideline update. As we have seen before, there are many concepts/terms of the medical terminologies such as SNOMED and UMLS have been extracted from guideline statements. They have been well represented in RDF N-Triples. Those semantic data can be stored in Triple stores and can be obtained by the semantic queries (e.g., SPARQL queries). Those extracted terms/concepts can serve as the basic keyword set for making the corresponding queries to find the relevant publications (e.g., evidences) for the consideration of the update on the guideline statement. We can also develop various methods to rank the terms/concepts in the basic keyword set, so that more important terms can be always selected than those less important terms based on the ranking. One of the interesting topics is to develop a semantic distance

measure for the terms/concepts ranking. Currently we are now working on a semantic distance measure between two terms based on their co-occurrence at the same publication in PubMed. The initial experiments have shown that this semantic distance measure can achieve better results for finding relevant evidences of medical guideline for guideline update [13].

The guideline update has been considered to be one of the tasks in the European 7th framework project EURECA. The main idea of the guideline update is to develop the methods so that new evidences can be found more efficiently.

We have implemented a guideline update system in SemanticCT (A Semantically Enabled System for Clinical Trials) [10,14,15]. That guideline update interface in SemanticCT provides various selections for guideline designers and other researchers to find relevant research evidences on guideline content, alternatively called guideline items, or conclusions. The interface provides the selection options to select the formalized evidence-based medical guidelines with different topics (e.g. subsection title of the guideline document). For each selected topic, the interface will show a list of the guideline items with their evidence levels, refereed literature and their evidence classes. The guideline update component is the tool that helps the guideline developers to search for relevant literature for update. The tool gives support for formulating the query. The user can select a guideline item, and then select different functionalities to check relevant literatures. Those functionalities include: finding

relevant research findings with different options on temporal aspects, such as “latest” new findings or findings in a specific year, and others.

We select the Dutch Breast Cancer Guidelines (version 2.0), which has been published in 2012 and the Dutch Breast Cancer Guidelines (version 1.0), which has been published in 2004, as the test data. We have generated the complete set of the guideline items in those two Dutch Breast Cancer Guidelines into the RDF N-Triple formats, and loaded them into the data layer of the LarKCplatform [15] and make them integrate with SemanticCT. We have made some initial experiments of finding evidences for the Dutch Breast Cancer Guidelines of both version 1.0 and version 2.0.

A screenshot of the guideline update interface in SemanticCT is shown in Fig. 1. In the interface the users can select a guideline (e.g., either Dutch Breast Cancer Guideline 2012, or Dutch Breast Cancer Guideline 2004). The system will show a set of the topics of the selected guideline and their corresponding guideline items (e.g., guideline conclusions). For each selected guideline item, the users can select the functions such as finding relevant evidences or trials for selected guideline item (with or without context). By the context we mean that the system will add the additional term from the topic to create a search query to find the relevant evidences or trials. The initial experimental results show that the semantic representation of those two evidence-based medical guidelines is potentially useful for medical applications such as guideline update and reasoning with evidences.

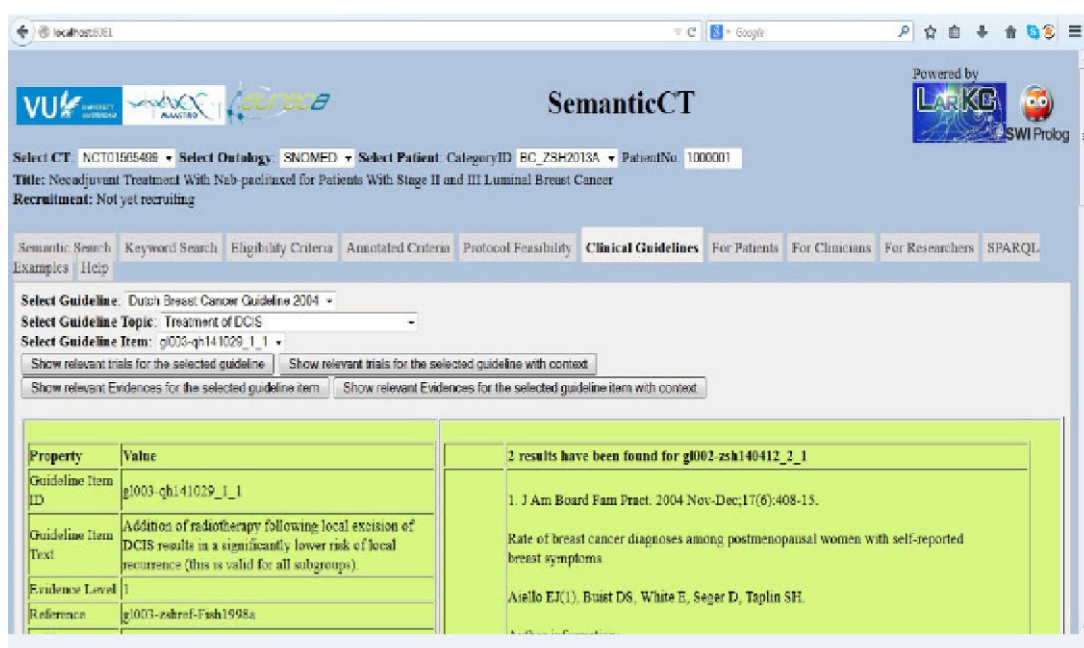


Fig. 1 Screenshot of the guideline update interface in SemanticCT

3 Conclusion

In this paper, we have discussed a semantic representation of EBM guidelines in which guidelines are represented as the Semantic Web standards such as RDF/RDFS/OWL. We have shown how to use the Xerox's NLP tool to make the semantic annotations of guideline statements with the well-known medical terminologies such as SNOMED and UMLS. We have presented some results of the semantic statements of those annotations with the concept identification and the relation extractions with evidence-based medical guidelines.

We have shown two kinds of use cases for the semantic representation of evidence-based medical guidelines. Reasoning with evidences in the first use case gives some methods for the correctness checking of evidence-based medical guidelines. The second use case of the guideline update show how the semantic representation of evidence-based medical guidelines can be used to find new and relevant findings for selected guideline conclusions.

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