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A Clinical Decision Support System based on Ontology and Causal Reasoning Models

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ABSTRACT

Clinical decision support system (CDSS) is promising in assisting physicians for improving decision-making process and facilitates healthcare services. In medicine, causality has become the main concern throughout healthcare and decision-making. Causality is necessary for understanding all structures of scientific reasoning and for providing a coherent and sufficient explanation for any event. However, there are lack of existing CDSS that provide causal reasoning for the presented outcomes or decisions. These are necessary for showing reliability of the outcomes, and helping the physicians in making proper decisions. In this study, an ontology-based CDSS model is developed based on several key concepts and features of causality and graphical modeling techniques. For the evaluation process, the Pellet reasoner is used to evaluate the consistency of the developed ontology model. In addition, an evaluation tool known as Ontology Pitfall Scanner is used for validating the ontology model through pitfalls detection. The developed ontology-based CDSS model has potentials to be applied in clinical practice and helping the physicians in decision-making process.

Keywords: *clinical decision support system, ontology, causality, causal reasoning, graphical modeling*

INTRODUCTION

Clinical decision support system (CDSS) is defined as a health information system designed to assist the physicians in decision-making process. CDSS is promising in assisting physicians for improving decision-making process and facilitate healthcare services. Nevertheless, it remains a challenge to successfully provide and implement CDSS in clinical practice. In medicine, causality have become the main concern throughout healthcare and decision-making (Hucklenbroich, 2014; Janke et al., 2016; Fischer et al., 2016; Islam et al., 2015). Causality is necessary for understanding all structures of scientific reasoning and for providing a coherent and sufficient explanation for any event. However, lack of existing CDSS that provide causal reasoning for the presented outcomes or decisions (Yet et al., 2017; Janke et al., 2016; Islam et al., 2015; Evans & Ossorio, 2018). These are necessary for showing the relevance and reliability of the outcomes, and helping the physicians in making proper decisions. As a result, the knowledge and clinical reasoning behind these systems are not explicable and disseminated even when they are based on strong evidence. These also may cause difficulties for the physicians to understand and assess the system's prospective performance as well as to convince them for accepting it in their clinical practice (Yet et al., 2017; Fischer et al., 2016; Islam et al., 2015).

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In this study, an ontology-based CDSS model is developed based on several key concepts and features of causality and graphical modeling techniques. The purpose of the CDSS model is to identify and visualize the causality in the clinical reasoning process. Ontology is a strong knowledge representation and communication model for intelligent agents (Lam et al., 2015; Sanchez, 2014). It is important to define and maintain expressive ontology for developing a CDSS. Semantics should be considered to develop a CDSS, since in healthcare each description should have a unique and understandable meaning (Lam et al., 2015; Sanchez, 2014). Besides, it can improve medical knowledge handling and reutilization as it facilitates faster knowledge access and gathering of relevant knowledge and evidence in supporting decision-making process (Lam et al., 2015; Sanchez, 2014). It also enables the system to be adaptive to clinical practice as it supports the knowledge repository to be updated and modified for incorporating new clinical cases or evidences into the system (Lam et al., 2015; Sanchez, 2014).

LITERATURE REVIEW

Ontology-based CDSS

The ontology-based CDSS consist of ontology as the knowledge base, which captures the domain knowledge in terms of a semantic representation of concepts, relationships and axioms (Jafarpour, 2013; Sanchez, 2014). A logic-based knowledge reasoner is used as the reasoning engine, whereby domain knowledge or information is represented in terms of instances of concepts and relations, and the output includes a set of conclusions or recommendations axioms (Jafarpour, 2013; Sanchez, 2014).

Causal Reasoning

Causality is intrinsic to human reasoning which involves the empirical relationship between a cause and its effect (Rovetto & Mizoguchi, 2015). Causality is necessary for understanding all structures of scientific reasoning and the decision making process (Hucklenbroich, 2014). It is also needed for providing a comprehensive explanation for any entity or event. There are several concepts and features of causality, such as in the followings:

- Causal direction indicates the direction of, an effect in a causal relationship (Ross, 2013). There are two kinds of causal direction, which are positive and negative direction A positive influence direction indicates that both factors change in the same direction (e.g. an increase causes an increase effect), while the negative influence indicates the opposite changes (e.g. an increase causes a decrease effect).
- Causal relationships can be represented in terms of whether the causal factor is a necessary or sufficient condition for an effect to occur (Gerstman, 2003; Katz, 2018). These concepts are commonly described in epidemiology aspects. Exposure is a term commonly used in epidemiology to denote any condition that is considered as a possible cause of disease (Gerstman, 2003).Exposure is considered necessary when it always precedes the effects (e.g. symptoms) and always presents when the effects occur (Gerstman, 2003). An exposure is considered sufficient when the effects become inevitable (Gerstman, 2003). In other words, a sufficient cause is a causal factor whose presence or occurrence guarantees the occurrence of symptom. There are four possibilities of necessity and sufficiency causes;
  1) Causal exposure E is considered both necessary and sufficient if (Gerstman, 2003):
     (i) Exposure E and disease D are always present together, and
     (ii) E acting alone inevitably leads to D ($E \rightarrow D$).
     In fact, this type of causality rarely occurs. It is strongly atypical for a single exposure to be a necessary and sufficient cause for a disease (Gerstman, 2003).
  2) Causal exposure E is considered necessary but not sufficient for disease D if (Gerstman, 2003):

(i) Exposure E is always present when disease D occurs
(ii) But D does not always occur in the presence of E
For example, *Mycobacterium* is necessary for tuberculosis (TB) Nevertheless, the tubercular bacterium is not always sufficient to cause the disease (Gerstman, 2003). It is possible for an individual to carry the bacterium in his/her body and remain asymptomatic (showing no symptoms). This implies that complementary factors (F) are needed for the disease to become manifest ($E + F \rightarrow D$). In the case of TB, the complementary factors include immunosuppression, genetic susceptibility, poor nutrition, multiple drug resistance, and failure to diagnose and treat throughout the TB asymptomatic stages (Gerstman, 2003).

3) Causal exposure E is considered not necessary but is sufficient for disease D if (Gerstman, 2003):
(i) D always occurs in the presence of E
(ii) But D is also able to occur in the absence of E
For example, Down syndrome is the most common cause of mental retardation (Gerstman, 2003). However, there are also other factors commonly cause the mental retardation, instead of Down syndrome, such as fragile X syndrome and foetal alcohol syndrome (Gerstman, 2003). As was the case in possibility 1, it is rarely for a single exposure to be a sufficient cause for a disease. This implies that there are other contributing factors that accompany Down syndrome in causing mental retardation (e.g. genetic causes, prenatal causes) (Gerstman, 2003).
4) Causal exposure E is neither necessary nor sufficient for disease D, if E might or might not precede D. In other words, E is a contributory cause that increases the likelihood of the occurrence of disease D. This implies that additional factors (F) is required to accompany E in causing D (Gerstman, 2003).
For example, cigarette smoking is neither necessary nor sufficient to cause lung cancer (Gerstman, 2003). Lung cancer may occur in the absence of smoking due to exposure to certain chemicals or gases (e.g. radon gas, asbestos, arsenic) (Jekel, 2007). Smoking is not by itself necessary or sufficient for developing lung cancer, People who smoke have high risk of lung cancer. The more people smoke, the more likely they are to develop lung cancer. The risk of lung cancer increases with the number of cigarettes smoked every day and the number of years that a person has smoked. Quitting at any age can significantly lower the risk of lung cancer (Jekel, 2007).

- Causal chain is a chain of entities linked by causal relations (Rovetto & Mizoguchi, 2015). It is a connected and ordered sequence of causal relationships between multiple factors (Ross, 2013). Causal chains typically consist of certain factor causing another, which then causes another. Visual representations of causal chains commonly use alphanumeric characters or shapes (i.e. nodes) for representing the factors, and then linked by unidirectional arrows for representing the causal relationship between them (Rovetto & Mizoguchi, 2015). There are three types of causal chain based on different causal scenarios; sequential, ongoing, and concurrent causal chain;

1) Sequential causal chain is an ordinary conception of causal chain that corresponds to non-cumulative process, which is a process that proceeds by completing the current process at every instant in time (e.g. < *accident happened* → *ambulance came* → victim *arrive at a hospital* >) (Kozaki et al., 2012).
2) Ongoing causal chain can be referred as cumulative continuous process, which is a process that proceeds without completing the current process at every instant in time (e.g. < angiostenosis → lack of oxygen in myocardial cells → necrosis of myocardial cells >) (Kozaki et al., 2012). Angiostenosis is an abnormal narrowing of a blood vessel that commonly occurs when the cholesterol plaques build up on the artery walls (Kozaki et al., 2012). These factors result in blood flow interruption and oxygen deprivation in myocardial cells. Then these causing necrosis (or death) in the heart muscle, which is also known as myocardial infarction or heart attack (Kozaki et al., 2012).
3) Concurrent causal chain is a chain, in which the causality process from the cause to the effect is occurring simultaneously throughout the chain (Rovetto & Mizoguchi, 2015). If the changes occur

simultaneously and without mediation, it is referred as pseudo-simultaneous causal chain (e.g. < collision → breakage >) (Rovetto & Mizoguchi, 2015). If the simultaneous causal chain involves mediation, it is referred as state-mediated causal chain (e.g. < growing blood clot → reduction of cross section of blood vessel → reduction in oxygen supply >) (Rovetto & Mizoguchi, 2015).

- Distal and proximal factors are another type of causal concept, which is particularly notable for the causal chain. The distal factors lie towards the beginning of causal chain (i.e. indirect causal factors), while the proximal factors lie towards the end of the chain (i.e. cause directly or almost directly the effect) (Liu et al., 2015).

Besides, graphic visualization is one of the basic approaches that has been employed, in order for improving the comprehension of cause-and-effect relationships (Greenland & Brumback, 2002). The graphical causal models able to illustrate the qualitative population assumptions, and the sources of bias, that are not easily noticed with other approaches (Greenland & Brumback, 2002). Causal graphs (or diagrams) are the most common visual representation of cause-and-effect relationships, which are a form of cognitive map that have emerged with numerous forms and structures (Ross, 2013). There are several forms of causal graphs including directed graph, Bayesian network (BN) and causal loop diagram (CLD).

- Directed graph is composed of vertices (or nodes) that represent the factors and targets, and the edges (line segment with arrowheads) that represent the causal relationships between them (Ross, 2013).
- BN is a graphical probabilistic model that represents the structure of data through a directed acyclic graph (Pellet, 2010: Yet et al., 2017). It is composed of nodes representing the variables and directed edges representing the relations or causal dependencies between the variables. Each variable has a set of parameters that are encoded by node probability tables for defining its probabilistic relation with its parents (i.e. conditional probability), or its prior probability if the variable does not have any parents (i.e. root node) (Pellet, 2010: Yet et al., 2017).
- CLD is a type of causal diagram that allows the illustration of cause-effect variables in the cyclical relationship (Belayutham et al., 2016; Ross, 2013). It consists of two components:
  1) Causal links between variables, which is represented by arrows. Each causal link is marked with polarity or causal direction (i.e. positive or negative influence direction) (Ross, 2013). A causal link is marked with delay (see Figure 1) if there is a significant delay between the cause and the effect. It is a situation where an occurrence of causal factor takes time for the effect to occur (Ross, 2013).
  2) Feedback loop, which represents the causal relationship as a loop (Ross, 2013). There are two kinds of feedback loop which are reinforcing (or positive) loop, and balancing (or negative) loop, and they are indicated by the number of negative causal links in a loop (Belayutham et al., 2016). The positive loop contains an even or zero number of negative causal links, while the negative loop contains an odd number of negative causal links (Belayutham et al., 2016). The positive loop is commonly labeled at the centre of the loop either by using the letter "R" or by using an icon of snowball rolling down a hill (see Figure 1) (Belayutham et al., 2016).. For the negative loop, it is labeled either by using the letter "B" or by using an icon of teeter-totter. In addition, a small looping arrow is usually drawn around the feedback loop label to indicate that the label refers to the feedback loop and to show the direction of the loop's rotation (Belayutham et al., 2016).

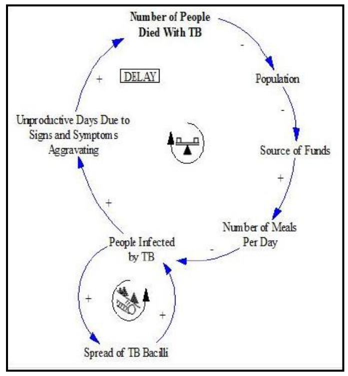

Figure 1: Example of CLD model of Tuberculosis (TB) case in Manila, Philippines (Bernardino & Datu, 2010)

RESEARCH DESIGN AND METHODOLOGY

This study adopts the approach proposed by Uschold and Gruninger (1996) for developing the ontology model. The development framework consists of four processes:

1) **Ontology Capture**: The ontology capture is part of the knowledge acquisition process. In this study, the ontology concepts are captured based on several literature searches and reviews. The concepts of causal reasoning are captured based on several features of causality and graphical modelling techniques including the directed acyclic graphs and causal loop diagram.
2) **Ontology Coding**: The ontology coding was performed using the Protégé-OWL editor and Pellet as the ontology reasoner. Protégé fully supports the latest OWL 2 Web Ontology Language and RDF specifications from the W3C. The OntoGraf plugin has been mainly used in this study for visualizing the relationships in the ontologies and organizing the structures of the ontology.
3) **Ontology Integration**: The integration of ontology refers to a process of reusing the existing ontology. It could be necessary to reuse the existing ontology in order to capture the previous established conceptualizations. In this study, the River Flow Model of Diseases (RFM) ontology has been adopted for capturing the concept of causal chain defined in this ontology. RFM is part of the Japan Medical Ontology Development Project for Advanced Clinical Information Systems. In this study, several of their ontology elements are adopted and modified for improving the ontology expressiveness and comprehensibility**.**
4) **Ontology Merging**: The ontology merging is the generation of new extended ontology from two or more sources of ontologies. Ontologies are developed at different levels of abstractions and details. Thus, it provides a holistic view of the domain area from several knowledge sources and collectively completes each other. The merging approach for this study consists of several steps;
   (i) Analyze the ontologies to be merged or check for similarities through analyzing their classes, properties and restrictions,
   (ii) Merge the ontologies by using the Protégé merge tool (i.e. merge ontologies option from refactor menu),
   (iii) Check the consistency of the merged ontology via running a reasoner and/or perform modifications for removing the presented inconsistencies or similarities.

   In this study, the ontology model is initially consists of two ontologies. The Causal Ontology 1 (CO1) represents the key concepts and features of causality, whereas the Causal Ontology 2 (CO2) represents the reuse of RFM ontology for modeling the causal chain concepts. The CO1 and CO2 ontologies are then merged into an extended causal ontology for extracting and relating the causal concepts from both ontologies.

DESCRIPTIONS OF ONTOLOGY MODEL

In this section, the ontologies are described in terms of OWL classes, properties, and instances. In order to easily recognized these terms in text, the OWL classes terms are italicized and in bold font (e.g**. *Class Name*)**, the properties terms are solely italicized (e.g. *property name*), and the instances are underlined and italicized (e.g. <u>*instance name*</u>). The followings provide the brief descriptions for the extended causal ontology model, which contains one main class (i.e. ***Causal Reasoning*** class). This class consists of two main subclasses for representing the corresponding causality concepts and features. The ***Causal Concepts*** class consists of five subclasses representing the concepts of necessity and sufficiency, distal and proximal causes, causal relation, causal direction, and causal chain concepts from RFM ontology.
The ***Causal Relation*** class describes the general types of relations in causality involving the relationship between at least two entities: cause and effect. From Figure 2(a), this class contains two subclasses representing two kinds of relations in causality: linear and cyclic causality (i.e. non-linear). Linear causality is a direct causal relation that has a clear beginning and clear end, in which a cause always precedes its effects (i.e. cause-effect) (Rovetto & Mizoguchi, 2015).

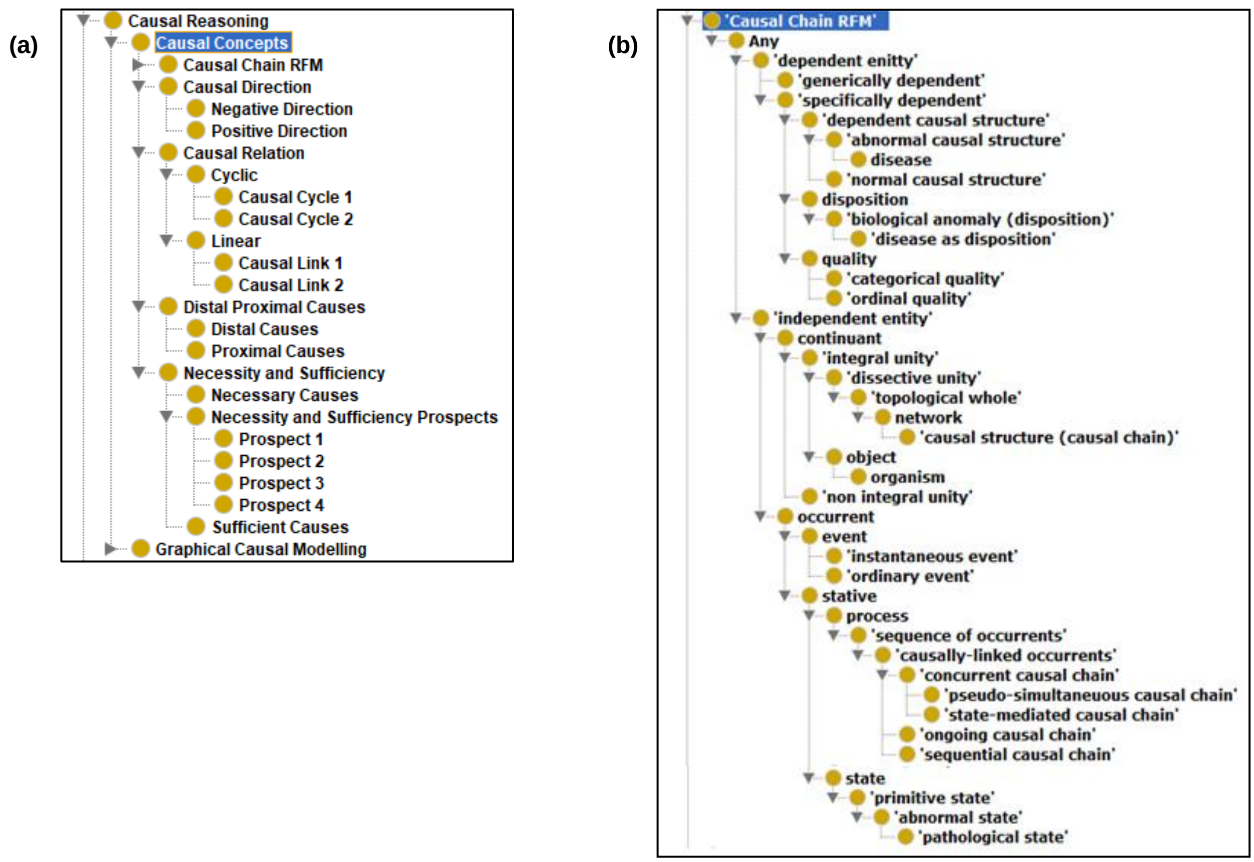

Figure 2: Class Hierarchy of (a) *Causal Concepts class* and (b) *Causal Chain RFM* subclass

On the other hand, the cyclic causality is an indirect causal relation, where a cause precipitates its effect, which in turn feeds back to affect the initial cause (i.e. cause-effect-cause) (Rovetto & Mizoguchi, 2015). There is no real beginning or ending in cyclic causality, as a cause can become an effect and vice versa. In addition, the linear causality can be characterized by the properties of asymmetry and inverse, while the cyclic causality can be characterized by the symmetry property (Rovetto & Mizoguchi, 2015). Both of these causalities can also be characterized by the irreflexive property, since this property is applicable to both of the causalities (Rovetto & Mizoguchi, 2015). Table 1 describes the features of these causalities.

As a result, several object properties are formed such as *causes* for the ***Linear*** class and *affects* for the ***Cyclic*** class in order to express the above-mentioned characteristics. Besides, from Figure 2(a), each of the subclass of ***Causal Relation*** class is then contains another two subclasses and several individuals for representing particular concepts of distal and proximal causes. The ***Causal Link 1*** and ***Causal Cyclic 1*** classes contain only the proximal (or directed) causes while the other two classes contain both distal and proximal causes.
Figure 3 shows a snapshot of OntoGraf of ***Causal Relation*** subclasses and several assertions of object properties for distinguishing between ***Linear*** and ***Cyclic*** classes. The rectangles with yellow circle represent the classes of the ontology, while the solid blue lines with arrowhead represent the hierarchy relationship between two classes (i.e. *has subclass*). The rectangles with purple diamond shape represent the individual of the class, while the solid purple lines denote the instantiation relation between the class and their individuals (i.e. *has individual*). Additionally, the dashed lines indicate the assertion of object properties between the classes or individuals.

Table 1: The features of linear and cyclic causality

LINEAR CAUSALITY	INVERSE PROPERTY	
	Causal Relation ***c causes e*** ***causes (c, e)***	**Inverse Relation** ***e is_caused_by c*** ***is_caused_by (e, c)***
	ASYMMETRY PROPERTY	
	causes (c, e) → ¬causes (e, c)	Effects do not cause their causes. If c causes e, then e does not causes c.
CYCLIC CAUSALITY	SYMMETRY PROPERTY	
	causes (c, e) → causes (e, c)	Effects do cause their causes. If c causes e, then e also causes c.
LINEAR & CYCLIC CAUSALITY	IRREFLEXIVE PROPERTY	
	Relata do not cause themselves	
	¬causes (c, c) ***¬causes (e, e)***	c does not cause c e does not cause e
Note: Italicized terms denote the predicates, '*c*' and '*e*' denotes the relata / cause and effect		

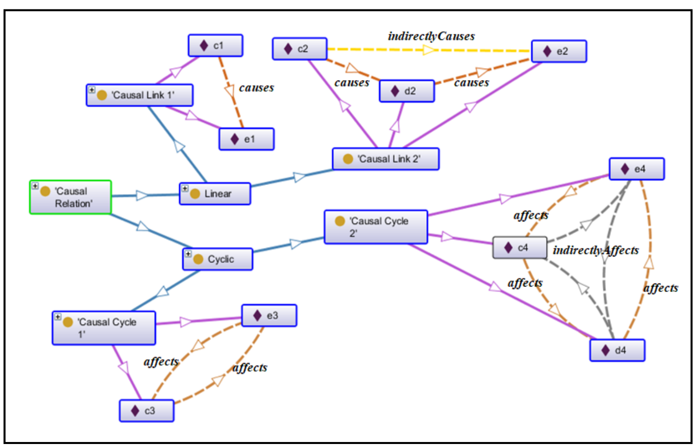

Figure 3: OntoGraf of *Causal Relation* class

Furthermore, the other subclasses of ***Causal Concepts*** class represent the key concepts and features of causality that have been described in previous section. The ***Causal Chain RFM*** class is integrated with RFM ontology for capturing their causal chain concepts. Several of their ontology elements are adopted and modified in this class for improving the ontology expressiveness and comprehensibility. From Figure 2(b), the ***causal structure (causal chain)*** class represents the concept of causal chain from RFM ontology. Rovetto and Mizoguchi (2015) defined that causality and causal chains are independent of any particular theory. Therefore, they classified that the causal chain is an independent entity and a type of continuant in the ontology. Besides, they also defined that the causal chain is constituted of occurrent, particularly in the types of sequence of occurrents, such as the causally linked-occurrents. Continuant can be defined as an object-like entity that enacts a process, while the occurrent is a processual entity that occurs or unfolds through time. As a result, a class named ***causally-linked occurrents*** is formed for capturing these concepts, and this class contains several subclasses representing different types of causal chains. The ***ongoing causal chain*** class is added in this study, while the other classes are adopted and/or modified from RFM ontology. Figure 4 shows the OntoGraf for the example of object properties assertions in the associated subclasses of ***Causal Concepts*** class. Several object properties are asserted for expressing particular causal relationships. The ***causal structure (causal chain)*** class represents the concept of causal chain (i.e. from ***Causal Chain RFM*** class), and the object property *isFormedOf* is asserted for expressing the classes that are related with the causal chain concept. In addition, the *hasCausality* property is asserted between the classes that have associated causal concepts.

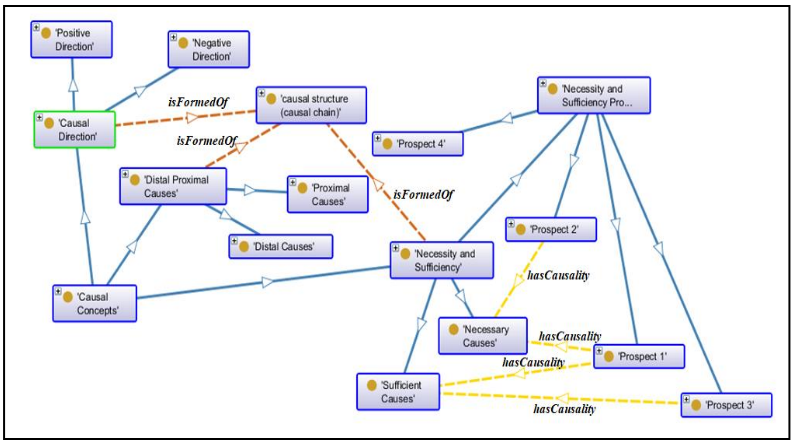

Figure 4: OntoGraf of other subclasses of *Causal Concepts* class

Subsequently, the ***Graphical Causal Modelling*** class represents the graphic visualization techniques in causal modeling, and consists of two subclasses representing different kind of visualization techniques; ***Causal Loop Diagram*** and ***Directed Graph*** classes. These classes are related with some of the ***Causal Concepts*** subclasses for expressing particular causal relationships. Figure 5 shows the OntoGraf for the example of asserted object properties in these classes. The dashed arrow with equal sign represents the equivalence class expression (i.e. *EquivalentTo*).

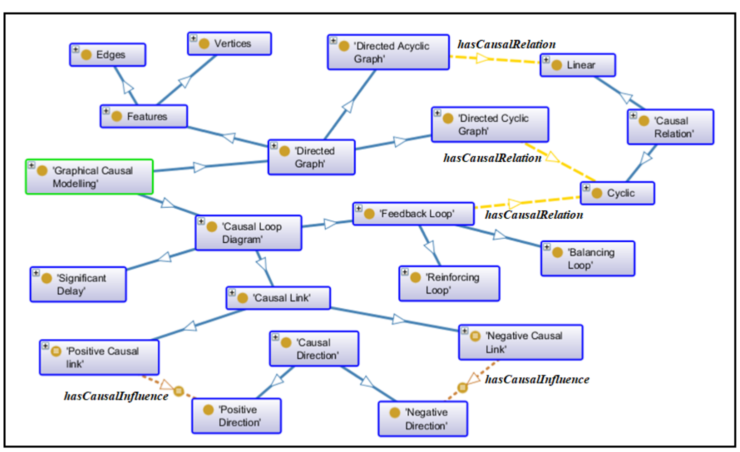

Figure 5: OntoGraf of other subclasses of *Graphical Causal Modelling* class

EVALUATION AND DISCUSSION

Generally, ontology evaluation is the task of measuring the quality of ontology in respect to particular criteria (Vrandečić, 2010). The aim of the evaluation process is to determine i) what the ontology defines correctly, ii) what it does not define, and iii) what it defines incorrectly (Poveda-Villalón et al., 2015). The ontology evaluation can be categorized in the context of two concepts; verification and validation. Ontology verification refers to the task of evaluating if the ontology was built in the right way, while ontology validation refers to the task of evaluating if the right ontology was built (Vrandečić, 2010).

In this study, as regards verification, Pellet reasoner is used to evaluate the consistency of the developed ontology model. This reasoner verifies whether there are any logical contradictions in the ontology axiom. In addition, an evaluation tool known as Ontology Pitfall Scanner (OOPS) is used for validating the ontology model. One approach for validating the ontology is to check whether the ontology contain anomalies (or pitfalls) (Poveda-Villalón et al., 2015). In OOPS, the ontologies are measured relatively to several dimensions and criteria: i) classification by dimension (structural, functional, and usability profiling dimensions); and ii) classification by evaluation criteria (consistency, completeness, and conciseness) (Poveda-Villalón et al., 2015). In this study, multiple OOPS scans were performed, since the evaluation of an ontology is an ongoing and continuous process during development and engineering of ontology. Several pitfalls were detected by OOPS, including critical, important, and minor pitfalls. For each detected pitfall, its code and description are indicated in order to identify where and why the pitfall occurs. Other useful information is also needed for understanding its implications and the way to fix it. Table 2 shows the examples of the pitfalls that are detected by OOPS in the developed ontology model.

Table 2: Examples of Detected Critical, Important, and Minor Pitfalls by OOPS

<table>
<tr><th colspan="2">P31: DEFINING WRONG EQUIVALENT CLASSES</th></tr>
<tr><td>Importance level : Critical</td><td rowspan="4">Solution approach (Poveda-Villalón, 2016):
Check whether the two classes are equivalent or not.
If not, the assertion of owl:equivalentClass should be removed.
Another type of relationship might hold between the classes.
E.g. hierarchical relation (rdfs:subClassOf) or mereological relation (i.e. assertion of object property to link both classes).</td></tr>
<tr><td>Aspects: Wrong inference</td></tr>
<tr><td>Affects: Classes</td></tr>
<tr><td>Reason:
Two classes are defined as equivalent, using owl:equivalentClass, when they are not necessarily equivalent.</td></tr>
<tr><th colspan="2">P11: MISSING DOMAIN AND/OR RANGE IN PROPERTIES</th></tr>
<tr><td>Importance level : Important</td><td rowspan="4">Solution approach (Poveda-Villalón, 2016):
For each object or data property without a domain, it is recommended to answer the following question for identifying its domain (i.e. what is the most general class in the ontology whose instances could serve as subject of the property?). The class that represents the answer can be defined as the domain for the property.
For defining a range for an object property, the class whose instances could serve as object of the property, can be used to define as a range for the property.
A range for a data property can be defined based on the format of the data or datatypes (e.g. integer, double, string).</td></tr>
<tr><td>Aspects: No inference,
Ontology understanding</td></tr>
<tr><td>Affects: Object properties,
Data properties</td></tr>
<tr><td>Reason:
The domain and/or range for object and/or data properties are not declared in the ontology.</td></tr>
<tr><th colspan="2">P08: MISSING ANNOTATIONS</th></tr>
<tr><td>Importance level : Minor</td><td rowspan="3">Solution approach (Poveda-Villalón, 2016):
(i) Include the label annotation properties (e.g. rdfs:label) for providing the terms that identify the ontology elements.
(ii) Include the description annotation properties (e.g. rdfs:comment) for providing the natural language definitions of the ontology elements.</td></tr>
<tr><td>Aspects: Ontology understanding,
Ontology clarity</td></tr>
<tr><td>Affects: Classes, Object properties,
Data properties</td></tr>
</table>

Reason: The ontology elements lack of annotation properties that label or define them.	

CONCLUSION

This study has developed an ontology-based CDSS model based on several key concepts and features of causality and graphical modeling techniques. For the evaluation process, the Pellet reasoner is used to evaluate the ontology consistency, whereas OOPS is used for validating the ontology through pitfalls detection. The developed ontology-based CDSS model can be further applied for assisting the physicians in comprehending the reasoning process and determining the effective decisions in practice.

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