Development of a Gestational Diabetes Computer Interpretable Guideline using Semantic Web Technologies

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Abstract: The benefits of following Clinical Practice Guidelines (CPGs) in the daily practice of medicine have been widely studied, being a powerful method for standardization and improvement of medical care quality. However, applying these guidelines to promote evidence-based and up-to-date clinical practice is a known challenge due to the lack of digitalization of clinical guidelines. In order to overcome this issue, the use of Clinical Decision Support Systems (CDSS) has been promoted in clinical centres. Nevertheless, CPGs must be formalized in a computer interpretable way to be implemented within CDSS. Moreover, these systems are usually developed and implemented using local setups, and hence local terminologies, which causes lack of semantic interoperability. In this context, the implementation of Semantic Web Technologies (SWTs) to formalize the concepts used in guidelines promotes the interoperability and standardization of those systems. In this paper, an architecture that allows the formalization of CPGs into Computer Interpretable Guidelines (CIGs) supported by an ontology in the gestational diabetes domain is presented. This CIG has been implemented within a CDSS and a mobile application has been developed for guiding patients based on up-to-date evidence based clinical guidelines.

1 INTRODUCTION

Clinical practice is based on the latest and most reliable clinical evidence to provide the best healthcare to patients. During the last years, studies have shown the benefits of following Clinical Practice Guidelines (CPGs) in the daily practice of medicine (Grimshaw and Russell, 1993), being a powerful method for standardization and improvement of the medical care quality. According to the Institute of Medicine's (IOM) definition, CPGs are "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" (Institute of Medicine, 1990).

However, applying these guidelines to promote the best evidence-based and most up-to-date clinical practice is a known challenge. There is a lack of digitalization of the guidelines, which makes it difficult to maintain them updated in a dynamic way and implement them in computerized systems.

In order to overcome these issues, Clinical Decision Support Systems (CDSS) that formalize guidelines in a computer interpretable way (i.e. as Computer Interpretable Guidelines or CIGs) are promoted. In this context, the application of Semantic Web Technologies (SWTs) to formalize the guidelines' concepts could be a key to promote the interoperability and standardization of the clinical knowledge, by giving the opportunity to pursue a reuse of ontologies.

In this paper, an architecture that will allow the formalization of CPGs into CIGs, supported by an ontology to assure a semantic validity of all the formalized information is presented. As a use case, the implementation of a gestational diabetes CIG is described. Moreover, a mobile based application is presented as the front-end of the CDSS for a patient-oriented guidance.

This paper is organized as follows. Section 2 describes the state of the art done about the different concepts needed in this work. Section 3 introduces the

methodology used during the development of the work. Section 4 explains a practical scenario, and finally, Section 5 presents our conclusions and future guidelines.

2 STATE OF THE ART

In this chapter, the state of the art in Semantic Web Technologies (SWTs), Clinical Practice Guidelines (CPGs) for Gestational Diabetes Mellitus (GDM) domain, Computer Interpretable Guidelines (CIGs), and Clinical Decision Support Systems (CDSS) is described.

2.1 Semantic Web Technologies (SWTs)

The technological breakthrough in biomedical engineering and health informatics is producing a huge amount of data coming from different sources, which causes a limited interoperability of healthcare systems (Kolias et al., 2014). The Semantic Web[1] is a Web of data that wants to enable computers to interpret and process information on the World Wide Web. SWTs provide the tools to process the data in a more effective way, create the framework for interoperability between systems and integrate data from various sources.

In this context, many researchers have made use of these technologies to cope with problems related to semantic interoperability of ontologies or clinical datasets. As an example, the work presented by El-Sappagh et al. (El-Sappagh et al., 2018) introduced the Diabetes Mellitus Treatment Ontology (DMTO) as a basis for shared-semantics, domain-specific, standard, machine-readable, and interoperable knowledge relevant to type 2 diabetes mellitus (T2DM) treatment. However, to the best of our knowledge, there is no available gestational diabetes-centered ontology in the main open source ontology repositories, such as BioPortal[2].

As can be seen, ontologies are becoming an important tool in the field of semantics for interoperability. In this sense, there are different ontology languages available for representing information on the semantic web, such as RDF Schema or Web Ontology Language (OWL). RDF Schema allows to build a simple hierarchy of concepts and properties, while OWL has the ability to

specify far more about the properties and classes, adding semantics to the schema (e.g. defining two concepts as equivalent or inferring implicit facts).

One of the widely used ontology editors is Protégé (Musen, 2015), which is fully compatible with the latest OWL and RDF specifications. In Protégé, terminologies are represented using classes, slots, and facets (Noy and McGuinness, 2001), and it also allows the use of annotation properties for adding labels to the ontology classes and to link each concept with its definition in validated and available standard terminologies (e.g. SNOMED CT[3], LOINC[4], NCI Thesaurus[5], CIE-10-ES[6]). These permit the representation of the biomedical concepts with stable and unique codes, guaranteeing the interoperability of the implemented knowledge.

2.2 Clinical Practice Guidelines (CPGs)

CPGs are a set of criteria developed in a systematic way to help professionals and patients in the decision-making process, providing the latest evidence-based diagnostic or therapeutic options when dealing with a health problem or a specific clinical condition (Kredo et al., 2016). Over the past years, these CPGs have been widely used as part of CDSS by formalizing them as CIGs. Such CIG-based CDSS have demonstrated to be able to increase the chance of impacting clinician behaviour compared to using only narrative guidelines, as they provide updated patient specific clinical data and advises at the point of care (Latoszek-Berendsen et al., 2010).

Realizing that SWTs presented an increased awareness when trying to cope with semantic interoperability problems in ontologies, some other researchers studied their usage to represent computerized CPGs. For example, Hu et al. (Hu et al., 2015) and Huang et al. (Huang et al., 2014) discuss several use cases of semantic representation of evidence-based medical guidelines, showing that they are potentially useful for medical applications.

Due to our research interest, a state of the art in Gestational Diabetes Mellitus (GDM) CPGs was done. GDM is the most common metabolic disorder of pregnancy, defined as a glucose intolerance developed in the second or third trimester of pregnancy (American Diabetes Association, 2016). It confers an increased risk and complications during pregnancy for both mother and child, including

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[1] https://www.w3.org/standards/semanticweb/

[2] http://bioportal.bioontology.org/

[3] http://www.snomed.org/snomed-ct/five-step-briefing

[4] https://loinc.org/

[5] https://ncithesaurus-stage.nci.nih.gov/ncitbrowser/

[6] https://eciemaps.mscbs.gob.es/

cesarean delivery, shoulder dystocia, macrosomia, and neonatal hypoglycemia (The HAPO Study Cooperative Research Group, 2008). Furthermore, women with GDM have a substantially increased risk to develop type 2 diabetes and cardiovascular diseases after pregnancy (Bellamy et al., 2009; Sullivan et al., 2012). Therefore, strategies addressed to optimize management of GDM including effective prevention, and proper diagnosis and treatment are mandatory (Chiefari et al., 2017).

There are several guidelines based on best available and updated evidence for the GDM management, such as the ones developed by the National Institute for Health and Care Excellence (NICE) or the World Health Organization (WHO). These guidelines allow patient-centered decision support by following several criteria: (i) the measurement of clinical variables by the patient itself, (ii) the readability and ease of follow-up of the given recommendations, and (iii) the guideline ability to deal with the guidance of the three pregnancy stages (before, during, and after pregnancy).

After analysing the different guidelines for GDM management, the Queensland Clinical Guideline (Queensland Clinical Guidelines, 2015) was selected to be used as the backbone guideline, extended with the knowledge of several other guidelines in the domain.

But, as it is known, following multiple CPGs in parallel could result in statements that may interact with each other, such as giving conflicting recommendations. Furthermore, the impetus to deliver customised care based on patient-specific information, results in the need to be able to offer guidelines in an integrated manner. In order to deal with these problems, a harmonized patient-centered CPG was created and formatted as CIG, enabling the development of a CIG-driven CDSS.

2.3 Computer Interpretable Guidelines (CIGs)

Computer Interpretable Guidelines (CIGs) are formal representations of CPGs that can be executed to provide guideline-based decision support. One of the several well-known approaches for formally representing CIGs are the "Task-Network Models" (TNMs). These models structure the dependencies among actions as hierarchical networks that when fulfilled in a satisfactory way provide a recommendation.

There exist several proposals to cope with different clinical modelling challenges (Peleg et al., 2003), such as GLIF (Patel et al., 1998), PROforma

(Sutton and Fox, 2003), Asbru (Seyfang et al., 2002) or EON (Tu and Musen, 2001).

These types of CIG formalisms have been used in many projects over the past years. For instance, PROforma representation was used by Isern et al. (Isern et al., 2012) for their proposal of ontology-driven execution of CPGs. Eccher et al. (Eccher et al., 2014) implemented and evaluated an Asbru-based DSS for adjuvant treatment in breast cancer. In Peleg et al. (Peleg et al., 2014) web-based interactive clinical algorithms were developed based on GLIF formalism for the sequencing of tasks to analyse patients with particular clinical conditions.

In this work, a simplified version of TNM was implemented based on inference rules (i.e. IF-THEN type rules), which is explained in Section 3.2.

2.4 Clinical Decision Support Systems (CDSS)

Realizing the potential of using CIGs and ontologies, most of the approaches in this field over the past years focus on guideline development and implementation for decision support. For instance, the work described in (Galopin et al., 2015) proposes an ontological reasoning method based on semantic web techniques to bring more flexibility to CDSS and offer the ability to deal with patients suffering from multiple pathologies by including several modelled CPGs. Another approach was done in (Riaño et al., 2012), where the contents of an ontology for the care of chronically ill patients were adapted to create individual intervention plans describing health-care general treatments and also to use it as the knowledge base of a decision support tool.

CDSS aim aiding clinicians in their decision-making process by providing the needed tools to analyse clinical data with latest evidence in the shortest time (Garg et al., 2005). However, they can also support patients in the management of different diseases. Advances in mobile communication for health care (m-Health) allow the design and development of patient-centric models to improve patient's self-management capabilities.

Recently, many studies have reported that computer-assisted expert systems, such as CDSS, might help diabetes practitioners and patients to make reliable diagnoses and management decisions (Balas et al., 2004; García-Sáez et al., 2014; Sun and Costello, 2018; Wilkinson et al., 2013). On the other hand, lifestyle plays an essential role in controlling diabetes, in both the prevention and management of the disease. Many reports in clinical research (Mottola, 2007; Padayachee and Coombes, 2015;

Silva-Zolezzi et al., 2017) support the theory that healthy eating and regular exercise are beneficial in both preventing GDM and improving pregnancy outcomes in women with GDM.

Taking this into account, among the different CDSS designed in recent years, the ones related to the management of GDM were analysed. For instance, in the work of Caballero-Ruiz et al. (Caballero-Ruiz et al., 2017) a web-based telemedicine platform for its use as CDSS for the management of GDM was designed to remotely evaluate patients, allowing them to upload their data at home. In addition, mobile applications allow using automatic processing tools to provide real-time advice based on monitoring data. Peleg et al. (Peleg et al., 2017) presented a personalized and patient-centric CDSS for the monitoring and evaluation of atrial fibrillation and gestational diabetes. A newer study (Miremberg et al., 2018) demonstrated the positive effect of a smartphone-based daily feedback system among women with GDM for improving patient compliance to treatment and a better control of glycaemic levels.

With the aim of going beyond the current state of the art of CPG-based CDSS, the objective of this project was to design a patient-centered mobile CDSS for the management of GDM with the novelty of integrating SWTs to the system.

3 METHODOLOGY

In this chapter, the methodology followed for the development of a semantically validated mobile CDSS for giving guidance to women in the management of Gestational Diabetes Mellitus (GDM) is described.

3.1 GDM Ontology

In this section, an ontology formalizing all concepts and knowledge coming from the different CPGs related to GDM prevention, management and treatment is presented. For this work, the Protégé editor was used to define the different gestational diabetes related clinical concepts and the relationships among them. This ontology was built using NCI Thesaurus terminology to assure a semantic interoperability of the knowledge. The big amount of biomedical concepts that NCI Thesaurus contains and the fact that it is open access makes it an appropriate terminology to be used for the GDM ontology. Besides, the Unified Medical Language

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System (UMLS)[7] code for each of the terminologies was also specified in the ontology. UMLS integrates the most notable vocabularies (e.g. SNOMED CT, ICD-10, etc.) in its repository. The result was then validated with a reasoner (Section 3.1.2) for ensuring a consistent ontology.

3.1.1 Ontology Formalization

All the conditions and rules expressed in the CIG contain variables and properties that are organized in an ontology with their specific names. This ontology is composed by a total number of 166 classes, which are separated in two main groups (Figure 1). The first group is under the class named *DMG360Concept* that comprises all the necessary variables' names for creating the CIG. The second group, named *DMG360Value*, compiles the classes that define the possible values of the classes from the first group.
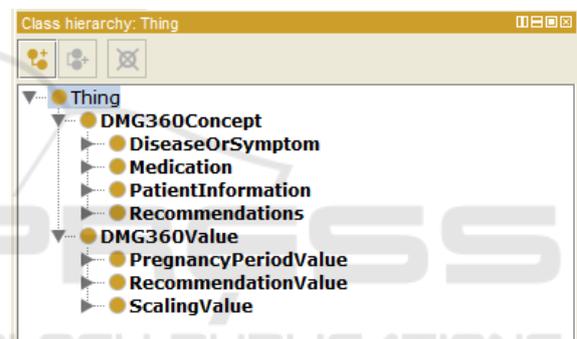
Figure 1: The two main groups of classes in the ontology: DMG360Concept and DMG360Value.

As can be seen in Figure 1, the group of concepts has four subclasses, and each of them comprises other subclasses. The first concept in the list (i.e. *DiseaseOrSymptom*) is composed by two subclasses: the *Disease* class, which contains two diseases definition (*DiabetesMellitus* and *PolycysticOvarianSyndrome*); and the *Symptom* class, with a list of 15 different symptoms as subclasses. The second concept (i.e. *Medication*) includes three subclasses corresponding to three different medications: *Antipsychotics*, *Corticosteroids*, and *Insulin*. The third one (i.e. *PatientInformation*) is the concept with the biggest number of subclasses, containing different information about the patient (e.g. information about maternal age, diabetes family history, ethnicity, physical activity, body mass index (BMI), etc.). The last concept (i.e. *Recommendations*) is related to the recommendations that are given to the user, which

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can vary depending on the stage of pregnancy, as explained in Chapter 3.2. In total, seven different types of recommendations are specified.

Furthermore, two different properties are defined within the ontology to relate the different classes and their values: a data property and an object property. Both are used to specify the range of values that can be taken by these classes, thus they are both defined using the noun *hasRange*. These ranges can handle either common data types (i.e. integer, Boolean…) when linked by a data property, or other possible values expressed as classes in the *DMG360Value* group when linked by an object property. For example, the *CurrentPhysicalActivityLevel* class is restricted to have a value corresponding to any subclass of the *ScalingValue* class (i.e. *High*, *Low*, or *Moderate*).

In addition, the clinical concepts' names, definitions and codes were extracted from NCI Thesaurus repository and defined within the model using annotation properties for its semantic standardization. Five different annotation properties were defined: (i) *NCI_label*, for giving the label of the class as stated in the NCI Thesaurus, (ii) *NCI_definition*, which contains the definition of the concept by the NCI, (iii) *NCI_code*, with the unique code of the term, (iv) *UMLS_CUI*, containing the corresponding UMLS code, and (v) *NCI_version*, specifying the version of the NCI Thesaurus repository used.

For the ontology design, OWL language was used. Having all the knowledge mapped, the model was exported in RDF language for the integration with the CDSS using the Jena API.

3.1.2 Ontology Validation

To validate the defined relationships between the variables and their possible values in the ontology, a tool called Reasoner was used. The reasoners offered by Protégé (i.e. FaCT ++, HermiT or Pellet) are programs that evaluate the consistency of an ontology by identifying relationships between classes. In this project, the FaCT++ reasoner was used.

After the triggering of this reasoner without obtaining any unsatisfactory relationship between the classes, the hierarchy of the designed GDM ontology was validated.

Moreover, the SPARQL Query tool in Protégé was used for the validation of the requests that could be done to the ontology in the process of its integration with the CDSS. For that, the SPARQL query language[8] was applied, a language that can be used to express queries across diverse data sources, whether the data is stored natively as RDF or viewed as RDF via middleware. Simple queries such as requesting data/object properties of a class, finding subclasses of a class, or showing the list of all classes in the ontology were tested.

3.2 GDM CIG

As stated in the state of the art, CPGs must be formalized in a computer interpretable way to provide guideline-based decision support and allow the evaluation of a patient in a computerized way. In this work, several CPGs with the clinical statements that describe the procedures to be followed in each clinical setup for the GDM management were studied and a more complete guideline that contained all the needed information for monitoring patients before, during and after pregnancy was created. This extended CPG was then formalized as IF-THEN rules in a computerized way (i.e. as a CIG) containing the concepts defined in the ontology.

Figure 2: Components of a Rule object used in this work.

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[8] https://www.w3.org/TR/sparql11-query/

To create the rules for this project, conditions (i.e. clinical statements to be accomplished) and their respective consequences (i.e. the recommendations to be given to the patient) were identified and extracted from the selected CPGs in the GDM domain. Once this knowledge was formalized in our extended CPG, a translation into computer interpretable language was done. For that, statements were translated into IF-THEN kind rules, where the conditional part is preceded by the IF expression and the consequent part by the THEN expression.

Each of the statements describing the criteria to be followed for guiding patients in this setup were defined as Rule objects, which encompasses (i) a conditional part composed by one or more conditions linked by (ii) a binary operator (i.e. *AND*, or *OR*) and (iii) a consequent part containing the recommendation for the patient, as can be seen in Figure 2. Each of the conditions is based on a Condition object, which stores (i) the name of the clinical variable to be evaluated (i.e. concept defined in the ontology), (ii) the mathematical operator (i.e. $>, \geq, =, <, \leq$) and (iii) the value or the threshold of the clinical variable to be evaluated. When the conditions of a rule are matching a patient's clinical information, a recommendation is provided to the patient.

Depending on the patient clinical stage, different types of interventions for the management of GDM were identified in the rule formalization process. For the stage before pregnancy, information about nutrition, physical activity and GDM risk factors were formalized. For the pregnancy period, guides related to nutrition, weight, physical activity, risk factors, and glucose control were covered. And finally, in the case of the post-pregnancy stage, nutrition, weight control, physical activity, breastfeeding, glucose control, and postpartum depression recommendations were included. The schema describing all this information is represented in Figure 3.

When formalizing this knowledge in the extended CPG and in its computerized version as CIG, the pipeline presented in Figure 3 was followed. The extended CIG contains 96 different rules distributed in three stages: 13 for the pre-pregnancy stage, 45 for the GDM management during pregnancy, and 16 for post-pregnancy stage. In addition, 22 characterization rules were also formalized, whose action is the change of variable values instead of providing a recommendation. These rules were not introduced into the CDSS as part of the rule base to be executed by the engine, but they were implemented in the mobile app itself.

3.3 Integration of the Ontology within the CDSS

Once the CIG was formalized with all computer interpretable rules and the GDM ontology was validated, the next step was to integrate both into the CDSS. For this objective, an authoring tool previously designed (Muro et al., 2019) was used. This tool enables an intuitive Graphical User Interface (GUI) for including new clinical knowledge
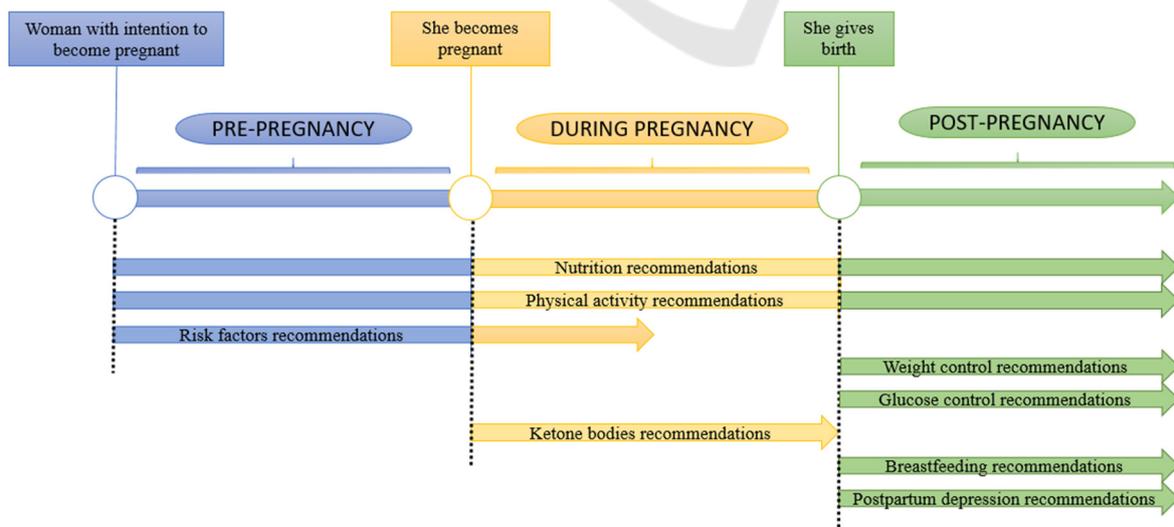
Figure 3: The three stages of pregnancy and the different recommendations giving in each of them.

in a computerized way into the CDSS rule base. A high-level project's architecture representation is shown in Figure 4.
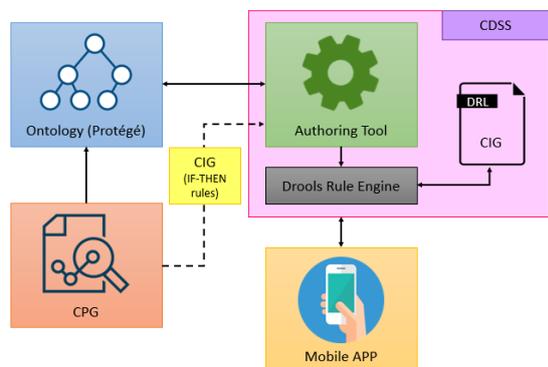
Figure 4: High level representation of the architecture of the project.

The development made within this project extended the authoring tool by introducing a new functionality: the syntactical and semantical validation of the formalized knowledge through an ontology. A research on different APIs (i.e. Protégé-OWL API[9], OWL API[10], Apache Jena[11], or RDF4J[12]) for the integration of ontologies in this kind of systems was done. After comparing them, Jena API was selected for carrying out the integration of the ontology with the Java based CDSS, because of its ease of use and compatibility advantages with our system.

In order to have an interaction between the GUI and the CDSS, different web services were developed as linkers to transmit data between them. These web services were used by the authoring tool (i) to get the list of variables (classes) for defining the evaluated variable name within a Condition object, (ii) to get the possible values of the specific variable selected in the Condition object, (iii) to get the list of recommendations for completing the consequent part of the Rule object, and (iv) to post each generated rule to the backend of the system. This backend is composed by different modules based on Drools[13], (i) a rule engine and (ii) a rule file generator in Drools Rule Language (.drl) extension.

To create the GDM CIG, each of the rules or conditions were introduced manually in the authoring tool using its GUI. In this process, four main blocks are fulfilled. First, the name of the rule is defined. Then, the conditions of the rule are introduced. Next,

the recommendation for the introduced rule is specified. And finally, the rule is sent to the backend.

In the second step for introducing the conditions of each rule, the Condition objects are constructed using the information obtained from querying the integrated ontology in the authoring tool. For requesting the filling out options, the previously described web services are used. In this context, the different types of ontology classes were used for different purposes, as explained below.
The classes of the ontology that correspond to the variables used for defining the conditional part of the CIG are under the *DMG360Concepts* class. These variables are requested and given as options for the first parameter of a Condition object in the authoring tool GUI.

Once the variable name of the Condition object is specified, the respective condition operator is selected. Then, in the third box for specifying the value or threshold of the selected variable, the authoring tool uses the web service for requesting its possible values, and here is where the second type of ontology classes interact. In the case of variables with data properties, the backend of the authoring tool defines the type of data that needs to be used by changing the format of the box in the GUI. For the case of the variables with object properties, a list containing subclasses of the group *DMG360Value* is given for being selected by the clinician.

Once the first condition is introduced, the binary operator can be selected from the given options (i.e. AND, or OR) and as many as required conditions can be defined within the conditional part of a single rule following the same procedure (see an example in Figure 5).
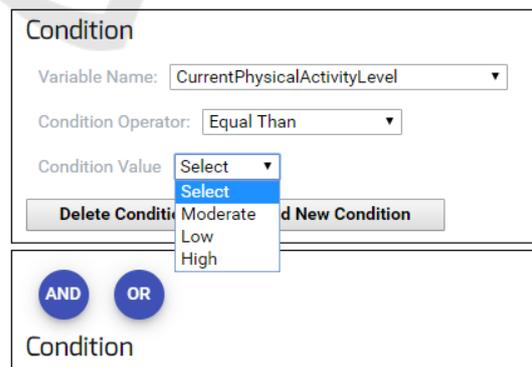
Figure 5: Example of the definition of rule conditional statements in the AT.

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[9] https://protegewiki.stanford.edu/wiki/ProtegeOWL_API
[10] https://github.com/owlcs/owlapi/wiki
[11] https://jena.apache.org/documentation/ontology/

[12] http://rdf4j.org/
[13] https://www.drools.org/

The third step of the introduction of the rule corresponds to the tab of the GUI for introducing recommendations, which permits the user to select the recommendation from a drop-down list. This list is the result of the request made by the authoring tool for the subclasses of the class *RecommendationValue* from the *DMG360Value* group in the ontology. When a recommendation is selected by the user using its name or abbreviation, the text corresponding to that recommendation is displayed above the selection box. Each of the texts for the respective recommendation class are specified in the ontology using annotation properties. The authoring tool uses a web service for obtaining the information from those annotations when a recommendation name is selected from the dropdown list.

Finally, the last step of the introduction of rules uses the fourth web service for sending the rules to the backend of the system and generating the .drl file, as explained above. This last web service takes all the values introduced by the clinician in the authoring tool and sends them to the backend, where they are processed and uploaded to the clinical database. As the structure of the objects generated in the authoring tool are the same as in the Rule object, a direct mapping can be done. The generated Rule object is then sent to the database, where it is stored, and then retrieved for sending it to the backend and generating the .drl file.

3.4 Patient-centered Mobile CDSS

Once the integration of the semantically validated CIG was implemented within the CDSS as a .drl file, a patient-centered mobile application was developed to interact with it. The user profiles defined for this application are (i) women that want to be pregnant and are monitoring their health status for it, (ii) women already pregnant, or (iii) women that have just given birth, and they all want to receive recommendations for managing the gestational diabetes. In the next lines, some examples of the different screens of the designed app and their functionalities are described.

First, a logging system was developed with registering or signing in options. This logging will save the basic personal data (i.e. sex, ethnicity…) that is supposed to be static during the monitoring period to avoid introducing it each time the user logs into the application.

Once the user is logged in, a main menu is displayed providing the possible user profiles to start the GDM management depending on their needs. Each of the pregnancy stages will provide specific recommendations, differing ones from the others as each period has a different focus on what to evaluate and how to treat the patient to reach her objective (see Chapter 3.2): in pre-pregnancy period, recommendations for nutrition, physical activity and GDM risk factors are given. During pregnancy, nutrition, weight, physical activity, risk factors, and glucose control related guidance is given. And for post-pregnancy period, nutrition, weight control, physical activity, breastfeeding, glucose control, and postpartum depression recommendations are given. This information is managed by the app through a menu, where for each stage different recommendations on the above stated topics can be provided.

Each time the user selects an option in the different menus, the variable corresponding to that specific topic is changed. For example, in the case of the menu for the post-pregnancy stage, when the user touches the image for obtaining recommendation concerning the glucose control, the variable GlucoseControlRecommendations is set to true.

If required, the application will retrieve more clinical information by questionnaires (see Figure 6). These questionnaires will ask for some questions that have possible answers to be selected. These answers are related to some clinical variables defined in the GDM ontology (mostly Boolean or Object property type variables), but sometimes it can require to the user introducing numerical variables' values (e.g. the blood glucose level). Every time she answers a question required in the app, this clinical information will be stored as part of her profile to be evaluated by the CDSS later.

Once all the questions for completing the needed patient profile are answered, they are sent to the CDSS in the backend, getting back the corresponding recommendation(s) to be displayed in the recommendation screen of the mobile application (see Figure 7).

4 PRACTICAL GDM SCENARIO

In this chapter a practical scenario is presented to show up how the whole architecture works. The selected patient profile represents a pregnant woman that would like to receive recommendations related to her glucose control. For that, she will be using the mobile application designed in this project. The presented clinical case is a non-diabetic pregnant woman that has suffered a decompensation in her Blood Glucose Level (BGL) with a glucose value of 136 mg/dL before eating (pre-prandial BGL). In

addition, her glucose levels showed higher values than the maximum threshold more than twice during the same week and in different intervals. Hence, her clinical data would be as follows:

Table 2: Clinical data of the patient profile for the use case.

Variable name	Value
DuringPregnancyPeriod	TRUE
GlucoseControlRecommendations	TRUE
GDM	FALSE
Type1Diabetes	FALSE
Type2Diabetes	FALSE
NormalBGLResults	FALSE
Insulin	FALSE
TwoOrMoreDecomp1Week	TRUE
InDifferentIntervals	TRUE
ExceedMaximumValues	TRUE
PrePrandialBGL	136

In the process for introducing these values in the mobile application, first the diabetes related questions are done to the user (i.e. the type of diabetes, and the glucose level value are requested). Then, some other questions are done to the user like (i) if she is taking insulin, (ii) if she had more than one decompensation of blood glucose levels in the same week, (iii) if they were in different intervals, and (iv) if they exceeded the maximum values. The screen of the app showing these questions is visualized in Figure 6.
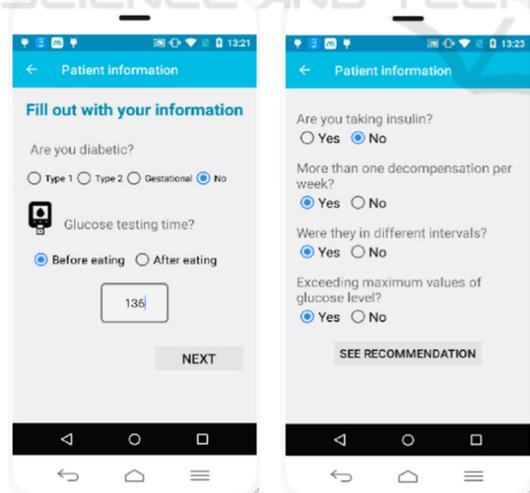
Figure 6: Questions of the questionnaire for glucose control in the mobile app.

Once this data is gathered by the system, it is sent to the backend to be evaluated by the CDSS. The rule(s) fitting the values of the variables sent by the user are triggered getting as result the recommendation corresponding to the matching rule. In this particular case, the recommendation obtained was: "Notify your doctor to consider insulin treatment" (see Figure 7).
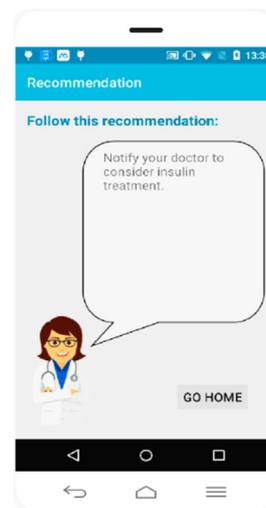
Figure 7: Recommendation screen in the mobile app.

Once the user receives the recommendation, she can follow it to solve her glucose level problem in this case. Besides, she can also go back to the menu and select other options for receiving recommendations about more interventions for the management of GDM.

5 CONCLUSIONS AND FUTURE WORK

CPGs have been promoted as a powerful method for standardization and improvement of medical care quality and personalization of healthcare. However, applying these guidelines to promote evidence-based and up-to-date clinical practice is a known challenge due to lack of digitalization of clinical guidelines. To overcome these issues, the use of semantic web technologies along with CDSS is proposed, in order to avoid the lack of semantic interoperability and promote the interoperability among systems in a standardized way.

In this paper, an architecture that allows the formalization of CPGs into Computer Interpretable Guidelines (CIGs) supported by an ontology in the gestational diabetes domain is presented. This CIG has been implemented within a CDSS to give support to the patients before, during, and after pregnancy. In addition, a mobile application has been developed for guiding patients based on up-to-date evidence based

clinical guidelines. This application is able to provide users different recommendations based on their clinical information.

As future work, applying tools for obtaining information from patients' electronic health records could optimize the efficiency of the designed mobile CDSS. In the same way, a more flexible way of gathering the user's clinical data will be implemented (e.g. using wearables for obtaining patient data without needing to introduce them manually). Likewise, a way to facilitate the ontology generation for clinicians will also be researched. Finally, it has been also envisioned the future inclusion of feedback tools within the mobile application in order to gather the user appreciation of the system, as well as the possibility to submit the system to the evaluation of clinical specialists.

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REFERENCES

American Diabetes Association, 2016. Classification and Diagnosis of Diabetes. *Diabetes Care 39, S13–S22*. https://doi.org/10.2337/dc16-S005

Balas, E. A., Krishna, S., Kretschmer, R. A., Cheek, T. R., Lobach, D. F., Boren, S. A., 2004. Computerized knowledge management in diabetes care. *Med. Care 42, 610–621*.

Bellamy, L., Casas, J.-P., Hingorani, A.D., Williams, D., 2009. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet Lond. Engl. 373, 1773–1779*. https://doi.org/10.1016/S0140-6736(09)60731-5

Caballero-Ruiz, E., García-Sáez, G., Rigla, M., Villaplana, M., Pons, B., Hernando, M. E., 2017. A web-based clinical decision support system for gestational diabetes: Automatic diet prescription and detection of insulin needs. *Int. J. Med. Inf. 102, 35–49*. https://doi.org/10.1016/j.ijmedinf.2017.02.014

Chiefari, E., Arcidiacono, B., Foti, D., Brunetti, A., 2017. Gestational diabetes mellitus: an updated overview. J. Endocrinol. *Invest. 40, 899–909*. https://doi.org/10.1007/s40618-016-0607-5

Eccher, C., Seyfang, A., Ferro, A., 2014. Implementation and evaluation of an Asbru-based decision support system for adjuvant treatment in breast cancer. *Comput.*

Methods Programs Biomed. 117, 308–321. https://doi.org/10.1016/j.cmpb.2014.06.021

El-Sappagh, S., Kwak, D., Ali, F., Kwak, K.-S., 2018. DMTO: a realistic ontology for standard diabetes mellitus treatment. *J. Biomed. Semant. 9*. https://doi.org/10.1186/s13326-018-0176-y

Galopin, A., Bouaud, J., Pereira, S., Seroussi, B., 2015. An Ontology-Based Clinical Decision Support System for the Management of Patients with Multiple Chronic Disorders. *Stud. Health Technol. Inform. 216, 275–279*.

García-Sáez, G., Rigla, M., Martínez-Sarriegui, I., Shalom, E., Peleg, M., Broens, T., Pons, B., Caballero-Ruíz, E., Gómez, E.J., Hernando, M.E., 2014. Patient-oriented Computerized Clinical Guidelines for Mobile Decision Support in Gestational Diabetes. *J. Diabetes Sci. Technol. 8, 238–246*. https://doi.org/10.1177/1932296814526492

Garg, A. X., Adhikari, N. K. J., McDonald, H., Rosas-Arellano, M. P., Devereaux, P. J., Beyene, J., Sam, J., Haynes, R. B., 2005. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. *JAMA 293, 1223–1238*. https://doi.org/10.1001/jama.293.10.1223

Grimshaw, J. M., Russell, I. T., 1993. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet Lond. Engl. 342, 1317–1322*.

Hu, Q., Huang, Z., Gu, J., 2015. Semantic representation of evidence-based medical guidelines and its use cases. Wuhan Univ. *J. Nat. Sci. 20, 397–404*. https://doi.org/10.1007/s11859-015-1112-y

Huang, Z., ten Teije, A., van Harmelen, F., Aït-Mokhtar, S., 2014. Semantic Representation of Evidence-Based Clinical Guidelines, in: Miksch, S., Riaño, D., ten Teije, A. (Eds.), *Knowledge Representation for Health Care. Springer International Publishing, Cham, pp. 78–94*. https://doi.org/10.1007/978-3-319-13281-5_6

Institute of Medicine, 1990. Clinical Practice Guidelines: Directions for a New Program. *National Academies Press (US), Washington (DC)*.

Isern, D., Sánchez, D., Moreno, A., 2012. Ontology-driven execution of clinical guidelines. *Comput. Methods Programs Biomed. 107, 122–139*. https://doi.org/10.1016/j.cmpb.2011.06.006

Kolias, V.D., Stoitsis, J., Golemati, S., Nikita, K.S., 2014. Utilizing Semantic Web Technologies in Healthcare. *Springer Int. Publ. Switz. 16*. https://doi.org/10.1007/978-3-319-06844-2_2

Kredo, T., Bernhardsson, S., Machingaidze, S., Young, T., Louw, Q., Ochodo, E., Grimmer, K., 2016. Guide to clinical practice guidelines: the current state of play. *Int. J. Qual. Health Care 28, 122–128*. https://doi.org/10.1093/intqhc/mzv115

Latoszek-Berendsen, A., Tange, H., Herik, H. J. van den, Hasman, A., 2010. From Clinical Practice Guidelines to Computer-interpretable Guidelines. *Methods Inf. Med. 49, 550–570*. https://doi.org/10.3414/ME10-01-0056

Miremberg, H., Ben-Ari, T., Betzer, T., Raphaeli, H., Gasnier, R., Barda, G., Bar, J., Weiner, E., 2018. The impact of a daily smartphone-based feedback system

among women with gestational diabetes on compliance, glycemic control, satisfaction, and pregnancy outcome: a randomized controlled trial. Am. *J. Obstet. Gynecol. 218, 453.e1-453.e7.* https://doi.org/10.1016/j.ajog.2018.01.044

Mottola, M.F., 2007. The role of exercise in the prevention and treatment of gestational diabetes mellitus. *Curr. Sports Med. Rep. 6, 381–386.* https://doi.org/10.1007/s11932-007-0056-1

Muro, N., Larburu, N., Torres, J., Kerexeta, J., Artola, G., Arrúe, M., Macía, I., Seroussi, B., 2019. Architecture for a Multimodal and Domain-Independent Clinical Decision Support System Software Development Kit. Presented at the *41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Berlin, Germany.*

Musen, M.A., 2015. The Protégé Project: A Look Back and a Look Forward. *AI Matters 1, 4–12.* https://doi.org/10.1145/2757001.2757003

Noy, N. F., McGuinness, D. L., 2001. Ontology Development: A Guide to Creating Your First Ontology 25.

Padayachee, C., Coombes, J. S., 2015. Exercise guidelines for gestational diabetes mellitus. *World J. Diabetes 6, 1033–1044.* https://doi.org/10.4239/wjd.v6.i8.1033

Patel, V. L., Allen, V. G., Arocha, J. F., Shortliffe, E. H., 1998. Representing Clinical Guidelines in GLIF. J. Am. *Med. Inform. Assoc. JAMIA 5, 467–483.*

Peleg, M., Fox, J., Patkar, V., Glasspool, D., Chronakis, I., South, M., Nassar, S., Gaglia, J. L., Gharib, H., Papini, E., Paschke, R., Duick, D. S., Valcavi, R., Hegedüs, L., Garber, J. R., 2014. A Computer-Interpretable Version of the AACE, AME, ETA Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules. Endocr. Pract. Off. J. Am. *Coll. Endocrinol. Am. Assoc. Clin. Endocrinol. 20, 352–359.* https://doi.org/10.4158/EP13271.OR

Peleg, M., Shahar, Y., Quaglini, S., Fux, A., García-Sáez, G., Goldstein, A., Hernando, M.E., Klimov, D., Martínez-Sarriegui, I., Napolitano, C., Parimbelli, E., Rigla, M., Sacchi, L., Shalom, E., Soffer, P., 2017. MobiGuide: a personalized and patient-centric decision-support system and its evaluation in the atrial fibrillation and gestational diabetes domains. *User Model. User-Adapt. Interact. 27, 159–213.* https://doi.org/10.1007/s11257-017-9190-5

Peleg, M., Tu, S., Bury, J., Ciccarese, P., Fox, J., Greenes, R.A., Hall, R., Johnson, P.D., Jones, N., Kumar, A., Miksch, S., Quaglini, S., Seyfang, A., Shortliffe, E.H., Stefanelli, M., 2003. Comparing Computer-interpretable Guideline Models: A Case-study Approach. *J. Am. Med. Inform. Assoc. 10, 52–68.* https://doi.org/10.1197/jamia.M1135

Queensland Clinical Guidelines, 2015. *Guideline: Gestational diabetes mellitus 38.*

Riaño, D., Real, F., López-Vallverdú, J.A., Campana, F., Ercolani, S., Mecocci, P., Annicchiarico, R., Caltagirone, C., 2012. An ontology-based personalization of health-care knowledge to support clinical

decisions for chronically ill patients. *J. Biomed. Inform. 45, 429–446.* https://doi.org/10.1016/j.jbi.2011.12.008

Seyfang, A., Miksch, S., Marcos, M., 2002. Combining diagnosis and treatment using ASBRU. *Int. J. Med. Inf. 68, 49–57.*

Silva-Zolezzi, I., Samuel, T. M., Spieldenner, J., 2017. Maternal nutrition: opportunities in the prevention of gestational diabetes. *Nutr. Rev. 75, 32–50.* https://doi.org/10.1093/nutrit/nuw033

Sullivan, S. D., Umans, J. G., Ratner, R., 2012. Gestational Diabetes: Implications for Cardiovascular Health. *Curr. Diab. Rep. 12, 43–52.* https://doi.org/10.1007/s11892-011-0238-3

Sun, S., Costello, K. L., 2018. Designing Decision-Support Technologies for Patient-Generated Data in Type 1 Diabetes. *AMIA. Annu. Symp. Proc. 2017, 1645–1654.*

Sutton, D. R., Fox, J., 2003. The Syntax and Semantics of the PROforma Guideline Modeling Language. J. Am. *Med. Inform. Assoc. JAMIA 10, 433–443.* https://doi.org/10.1197/jamia.M1264

The HAPO Study Cooperative Research Group, 2008. Hyperglycemia and Adverse Pregnancy Outcomes. *N. Engl. J. Med. 358, 1991–2002.* https://doi.org/10.1056/NEJMoa0707943

Tu, S.W., Musen, M.A., 2001. Modeling data and knowledge in the EON guideline architecture. *Stud. Health Technol. Inform. 84, 280–284.*

Wilkinson, M.J., Nathan, A.G., Huang, E.S., 2013. Personalized Decision Support in Type 2 Diabetes Mellitus: Current Evidence and Future Directions. *Curr. Diab. Rep. 13, 205–212.* https://doi.org/10.1007/s11892-012-0348-6