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A DECISION SUPPORT SYSTEM FOR DIABETES MEDICINE SELECTION USING PATIENT CENTERED TREATMENT BASED ON FUZZY LOGIC AND DOMAIN ONTOLOGY

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Abstract. *Diabetes not only imposes psychological and physical pain on patients but also has high medical costs. Thus, the prescription strategy of clinical doctors must consider many factors. In this paper, we develop an individualized antidiabetic drugs recommendation system for patients with diabetes. This system combines fuzzy logic and an ontology system which can be manipulated with relative ease, and targets reasonable HbA1c levels that address individual differences among patients. The system was evaluated by an endocrinologist and an attending physician. That indicated the antidiabetic drugs recommendation system has good performance and is useful both in 90%. The system also performs 80% for accuracy, that can assist clinicians in the management of diabetes mellitus during selecting drugs and the patient individualization HbA1c Target.*
Keywords: Fuzzy system, Type 2 diabetes, Domain ontology, Decision support system

1. **Introduction.** According to the International Diabetes Federation's 2015 data [1], the number of diabetes patients worldwide has reached 415 million affecting 1 in 11 adults. Without active intervention, by 2040 the number of diabetes patients worldwide will increase by 55% to 642 million or 1 adult in 10. In 2015, five million people died from diabetes-related complications which was one death every 6 seconds. The cost of treating diabetes worldwide is $673 US billion at the time of writing with 12% of global health expenditures dedicated to diabetes treatment and related complications. Notably, most of people with diabetes are with low and middle income in third world countries so diabetes has exerted a tremendous impact on the socio-economic development of these nations [1]. Thus, diabetes has a tremendous impact on both patients and national health insurance systems. Reducing costs and individualizing care are urgently needed.

HbA1c has become a standard clinical assessment of glycaemia and a standard part of diabetes management [2]. In 2015, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) [3] jointly issued a statement on Type 2 Diabetes Mellitus management (T2DM). It was suggested that clinical decisions were to be based on patient-centered care. In view of the uncertainty inherent in the therapeutic type and sequence, this method is especially suitable for patients with T2DM. The recommendation was to set patients' personal glycemic targets based on patient characteristics instead of the inflexible levels set by the ADA's "Standards of Medical

Care in Diabetes 2011" [4] which suggested that lowering *HbA1c* is less than 7% for most patients, while American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) suggested *HbA1c* be below 6.5% [5].

Ontology is one of important tools for the organization and representation of knowledge [6-9]. Ontologies are also usually used for knowledge sharing, update and reuse. Many of researches suggest that using ontologies build clinical guidelines and care plans [10-14]. In this paper, we will use the ADA and the EASD's statements to create a Glucose-Lowering Agents ontology and an antidiabetic drugs reasoning module to recommend antidiabetic drugs for patients.

However, ADA and the EASD's statements also describe seven factors for the clinician to determine ideal target value of *HbA1c* for patients with T2DM [3]. The factors include "risks potentially associated with hypoglycemia and other drug adverse effects", "disease duration", "life expectancy", "important comorbidities", "established vascular complications", "patient attitude and expected treatment efforts", "resources and support system". These factors are difficult to present by accurate numbers. So, it is better to use linguistic terms. For example, the "important comorbidities" can be divided into three levels: 'Absent', 'Few/Mild' or 'Severe'. The "resources and support system" can be divided into 'Readily available' or 'Limited'. Fuzzy logic is based on mapping real numbers to linguistic words of human language [15]. So we use the fuzzy logic to integrate domain ontology to build the ideal *HbA1c* target value inference module.

Finally, we create a drug recommendation system for diabetic patients that combines fuzzy logic with ontology reasoning. In order to make this system less complicated, we impose some restrictions. First, the system is only applicable to patients with type 2 diabetes. Second, only glucose-lowering drugs available in Taiwan are recommended.

The remainder of this paper is organized as follows. Section 2 presents the literature review. Section 3 introduces the overall structure and patient ideal *HbA1c* target inference module. Section 4 describes the actual verification system and glucose-lowering agents ontology and reasoning module. Experiments and system operations are discussed in Section 5. Conclusions are offered in Section 6.

2. **Literature Review.**

This research combines fuzzy logic and an ontology system to build a patient-centered treatment decision support system which can infer the individualization *HbA1c* target and recommend antidiabetic drugs for patients with T2DM. This section describes a brief description of Protégé and the study on related works of Clinical Decision Support System (CDSS), ontology and reasoning system.

2.1. **Protégé.**

Protégé (http://protege.stanford.edu) is free and open-source, it has been developing and managing by Stanford Center for Biomedical Informatics Research (BMIR) [16]. Protégé provides a graphic user interface and full support for editing the web ontology language. Protégé has become a popular tool to build knowledge [8,10-12,17-21].

2.2. **Ontology and reasoning systems.**

Ontologies contain the collection of medical definitions, treatment, drug information, patient physiological data that can be used in clinical decision support system [8]. Many researchers use health care knowledge to construct ontology and they build a reasoning system by inference rules based on expert knowledge. Bau et al. [17] used domain ontology and rule reasoning to construct a Clinical Decision Support System (CDSS) for diabetic patients undergoing surgery. By sharing the clinical knowledge of experts, data can be shared, updated, and reused through an ontology-based system. The system provides clinicians with evidence-based recommendations to promote medical quality.

Chen et al. [18] proposed a diabetes medication recommendation system based on domain ontology. The system employed the knowledge base provided by a hospital specialist in Taichung's Department of Health and the database of the American Association of Clinical Endocrinologists medical guidelines for clinical practice for the management of diabetes mellitus. The system builds ontology knowledge about the drugs' attributes and patients' symptoms and then it applies Java Expert System Shell (JESS) to inferring the most appropriate drugs.

2.3. **Clinical Decision Support System (CDSS).** Clinical Decision Support System (CDSS) is the provision of characteristics of an individual patient which is intelligently filtered by computerized clinical knowledge base. CDSS prioritized and presented at the right time to clinicians, patients, staff and others to enhance the patient health and health care [10,22]. Patients with Type 2 diabetes mellitus exhibit tremendous differences in phenotypes resulting of significant heterogeneity in clinical results. Clinical practitioners thus need to select different drugs to meet the needs of patients. However, the greater choices of clinical therapy may lack long-term research for therapeutic effects which needed to inform decision makers to imply uncertainty about the long-term benefits of new drugs. Vascular complications are a good example of the kind of problems that can occur [23-25]. Consequently, clinical practitioners cannot be certain whether a prescription for a specific patient is the best.

Ceriello et al. [26] investigated various performance types of patients. First, they referred to the patient's major characteristics, including *HbA1c*, Body Mass Index (BMI), occupational risk potentially related to hypoglycemia, chronic renal failure, and frail elderly status. Patients were divided into six groups, and each group had its own algorithm. By incorporating glucose self-monitoring levels, the study analyzed each patient's performance type. Finally, it provided patients with a gradual adjustment of glucose drugs. It is noteworthy that, to date, there has been no clinical evaluation of this study.

Ampudia-Blasco et al. [27] developed a decision supporting tool named DiaScope for patients with diabetes using expert's opinion-based systematic analysis. Research was focused on patients to whom metformin had been administered. These patients either had mal-control of glucose or Impaired Glucose Tolerance (IGT). The factors taken into consideration included therapeutic drugs administered, the gap between *HbA1c* and target level, risk of hypoglycemia, body mass index, average life expectancy, and complications. Their suggestions included a selection of second and tertiary glucose-lowering drugs, drug change, and replacement of drugs from impaired glucose tolerance to metformin. Concurrently, the study evaluated the adequacy of recommendations in terms of 'appropriate, inappropriate and uncertain'.

Although a number of researchers have considered the positive potential of CDSS [10,11,13,14,17,18,20,26,27], CDSS system did not consider patients' individual characteristics, for example, patients' attitude, resources, and support system effect positive treatment strategies or *HbA1c* targets. In addition, as time passes, there will be additional antidiabetic pharmaceutical options and new ideas to guide clinical practitioners to prescribe such as new medicine SGLT2 and injection medicine GLP-1.

In this paper, we will use ontologies to construct the drugs ontology and the patient ontology. Fuzzy logic is used to transfer ADA and the EASD's statements to human language. Next, we use the fuzzy logic to integrate domain ontology to build the ideal *HbA1c* target value inference module. The major contributions of the paper include (1) use fuzzy system to convert ADA and EASD's diabetic statements to fuzzy treatment system, (2) use ontology to construct patient center knowledge system, (3) integrate the

fuzzy and ontology system to do the reasoning, and (4) a drug recommendation system for diabetic patients is effective.

3. **The Framework of Recommendation System.** The recommendation system of this plan consists of three modules. The framework of the system is shown in Figure 1.

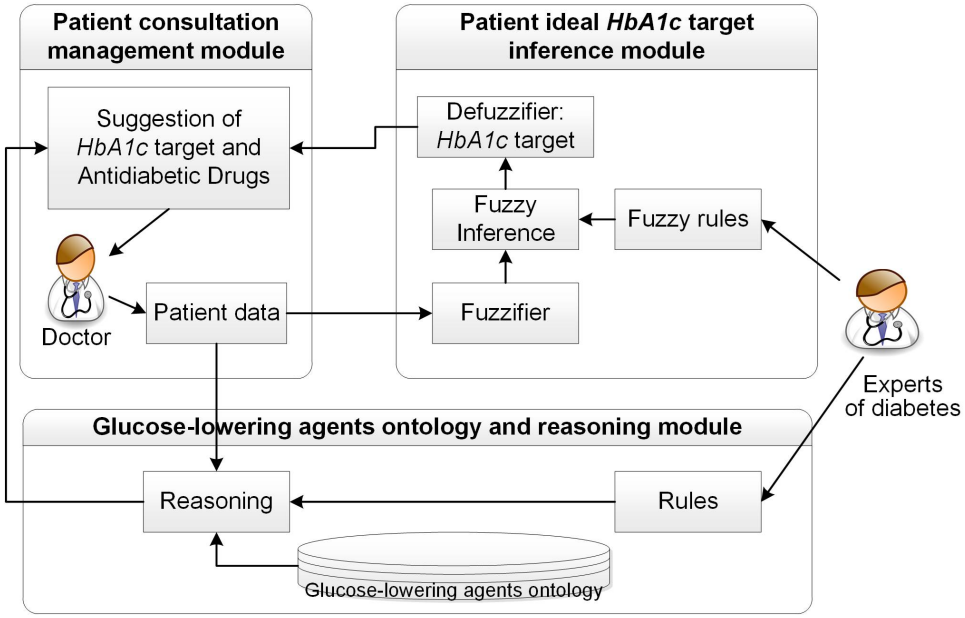

FIGURE 1. The framework of recommendation system

In Figure 1, the "Patient consultation management module" provides a user interface to clinical doctors. So, the clinical doctors can input patient's data from the interface. Those patients' data will be delivered to the other two modules. Next, the "Patient ideal *HbA1c* target inference module" will use fuzzy technology to infer the patient's individualization *HbA1c* target. Finally, the "Glucose-lowering agents ontology and reasoning module" will recommend antidiabetic drugs for patients. In this system, the fuzzy rules and ontology reasoning rules are set up by diabetes experts and clinical endocrinologists.

3.1. **Patient consultation management module.** According to the ADA and EASD statements [3], there are seven factors with depiction of patients and disease features that may be used by the clinician to determine ideal *HbA1c* target values for patients with T2DM. So, sufficient communication between the clinical doctor and the patient is necessary to evaluate seven factors: (1) the risks associated with hypoglycemia and other drug adverse effects, (2) disease duration, (3) life expectancy, (4) important comorbidities, (5) established vascular complications, (6) patient attitude and expected treatment efforts, (7) resources and support system. The clinical doctor also needs to record patient's history of diseases and Adverse Drug Reactions (ADRs).

3.2. **Patient ideal *HbA1c* target inference module.** There are seven inputs, namely $x_1, x_2, \ldots, x_7$, for fuzzy logic. Each of the input factors is divided into five levels, ranging from integers 0 to 4. The output value z is the ideal *HbA1c* target level, which takes individual differences into considerations. The membership functions play an important role for the fuzzy representation. Table 1 shows the names of the membership functions of input and output variables. In order to get the better results, we help the endocrinologist to establish patients' data and use Matlab/FuzzyLite toolbox to try and adjust the

TABLE 1. Names of membership functions of input and output variables

Variable	Name	Function1	Function2	Function3
x_1	risks potentially associated with hypoglycemia and other drug adverse effects	Low	High	–
x_2	disease duration	Newly Diagnosed	Long Standing	–
x_3	life expectancy	Long	Short	–
x_4	important comorbidities	Absent	Few/Mild	Severe
x_5	established vascular complications	Absent	Few/Mild	Severe
x_6	patient attitude and expected treatment efforts	Highly Motivated	Less Motivated	–
x_7	resources and support system	Readily Available	Limited	–
z	*HbA1c*	More Stringent	Mild Stringent	Less Stringent

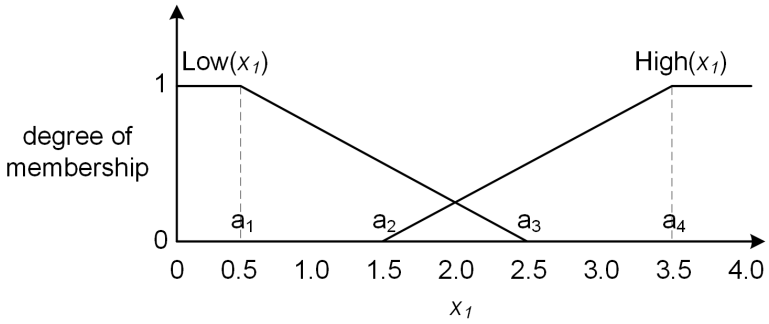

FIGURE 2. Membership functions of x_1 factor

parameters of the membership functions. Through the sufficient experience of clinician, the system has better results.

According to the ADA and EASD position statement [3], the "the risks associated with hypoglycemia and other drug adverse effects" can be divided into two levels: 'Low' or 'High'. So x_1 had two membership functions: Low(x_1) and High(x_1). The membership functions for Low(x_1) and High(x_1) are trapezoid. The ranges of x_1 membership functions are shown in Figure 2. Because x_2, x_3, x_6, and x_7 also can be divided into two levels, their membership functions are the same as x_1, and so on.

The "important comorbidities" can be divided into three levels: 'Absent', 'Few/Mild' or 'Severe'. So x_4 had three membership functions: Absent(x_4), Few_Mild(x_4) or Severe(x_4). The membership functions for Absent(x_4) and Severe(x_4) are trapezoid, and Few_Mild(x_4) is triangular. The ranges of x_4 membership functions are shown in Figure 3. Because x_5 also can be divided into three levels, x_5 membership functions are the same as x_4.

The American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) suggested *HbA1c* be below 6.5% [5], but the patient-centered care is needed to consider the patient's characteristics to set the patient's personal *HbA1c* target. So the output z represents the ideal *HbA1c* target, which varies between 6.5% and 9.0%. The output value z can be divided into three levels: 'More Stringent', 'Mild Stringent' or 'Less Stringent'. So z had three membership functions: MoreStringent(z),

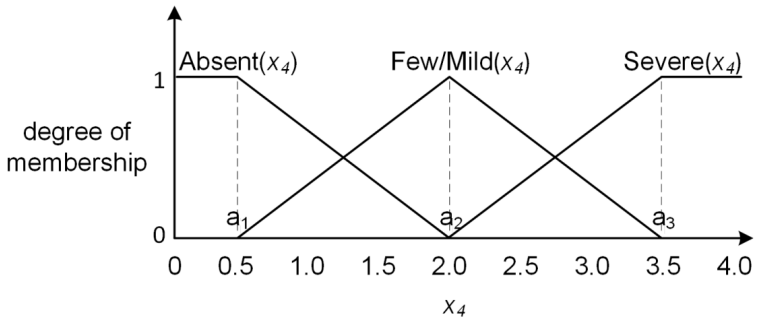

FIGURE 3. Membership functions of x_4 factor

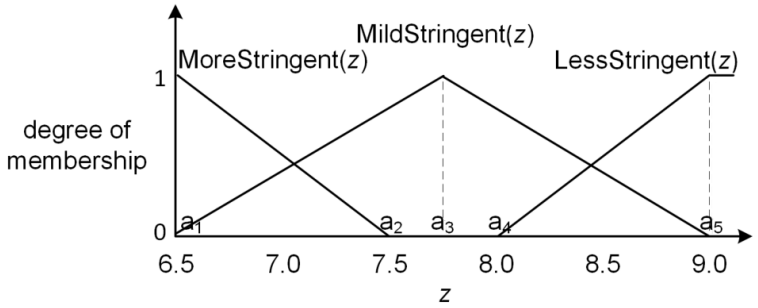

FIGURE 4. Membership functions of output z

MildStringent(z) or LessStringent(z). The membership functions for MoreStringent(z) and LessStringent(z) are trapezoid, and MildStringent(z) is triangular. The ranges of membership functions z are shown in Figure 4.

The second step is to apply inputs to the fuzzy rules. The fuzzy inference will then stipulate what action should be taken for each combination of sets of memberships. The main consideration for the method is relative safety of treatment. The number of fuzzy rules depends on several input factors. For example, if the clinical doctor inputs x_1, x_2, x_4 values, x_1 will have two membership functions (Low, High), x_2 have two membership functions (Newly Diagnosed, Long Standing), and x_4 will have three membership functions (Absent, Few/Mild, Severe) so the fuzzy rules consist of 12 individual rules. Based on individual expert's experience and intuition, the fuzzy rules table is shown in Table 2. Rule 1 indicates that if x_1 is low and x_2 is newly diagnosed and x_4 is absent, then z is more stringent. Rule 2 indicates that if x_1 is low and x_2 is newly diagnosed and x_4 is few/mild, then z is mild stringent. Otherwise, the output z is less stringent in rule 3-12 because x_1 is high, or x_2 is long standing, or x_4 is severe.

Finally, for both safety fuzzy rules and positivity fuzzy rules, the system uses the Mean of Maximum (MeOM) to perform defuzzification.

4. Glucose-Lowering Agents Ontology and Reasoning Module.

Protégé is a free software program for building ontology knowledge solutions [16], and Jess is the Java Rule Engine developed by Sandia National Laboratories [28]. We integrate Protégé 3.4.4 with the Jess plugin to evaluate the ontology and reasoning module. The details are as follows.

4.1. Glucose-lowering agents ontology.

In 2015, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) published an update of the position statement on management of Hyperglycemia in Type 2 Diabetes [3]. Using this position statement, we create a glucose-lowering agent ontology. The

TABLE 2. Example of fuzzy rule table

Rule	x_1	x_2	x_4	z
1	Low	Newly Diagnosed	Absent	More Stringent
2	Low	Newly Diagnosed	Few/Mild	Mild Stringent
3	Low	Newly Diagnosed	Severe	Less Stringent
4	Low	Long Standing	Absent	Less Stringent
5	Low	Long Standing	Few/Mild	Less Stringent
6	Low	Long Standing	Severe	Less Stringent
7	High	Newly Diagnosed	Absent	Less Stringent
8	High	Newly Diagnosed	Few/Mild	Less Stringent
9	High	Newly Diagnosed	Severe	Less Stringent
10	High	Long Standing	Absent	Less Stringent
11	High	Long Standing	Few/Mild	Less Stringent
12	High	Long Standing	Severe	Less Stringent

TABLE 3. Classes in the domain ontology

Class	**Description**
Glucose-Lowering_Agents	Concepts about glucose-lowering drugs. Ontology content is based on the ADA/EASD's position statement on management of Hyperglycemia in Type 2 Diabetes to be established.
Glucose-Lowering_ Advantages	Concepts about glucose-lowering advantages
Glucose-Lowering_Cellular_ mechanisms	Concepts about glucose-lowering cellular mechanisms
Glucose-Lowering_ Compounds	Concepts about glucose-lowering compounds
Glucose-Lowering_Cost	Concepts about glucose-lowering cost
Glucose-Lowering_ Disadvantages	Concepts about glucose-lowering disadvantages
Glucose-Lowering_Primary_ physiological_actions	Concepts about glucose-lowering primary physiological actions
Patients	Concepts about patient's profile, the properties include patient's adverse drug reactions (ADRs) and history of diseases.

classes and the descriptions of their concepts in the domain knowledge are shown in Table 3.

Classes can contain individual objects called instances. Object properties represent relationships between two instances, and each property has a domain and a range. Table 4 presents some of the object properties in the ontology. After classes and object properties are created, we build glucose-lowering agent instances based on the ADA/EASD's position statement on management of hyperglycemia in Type 2 diabetes.

4.2. **Antidiabetic drugs reasoning module.** Jess is a rule inference engine running on the Java platform [28]. This study developed SWRL rules for reasoning in which glucose-lowering agents are not suitable for patients. The two of rules are used as detailed below.

TABLE 4. The object properties in the ontology

Object Property Name	Domain	Range
has_Advantages	Glucose-Lowering_Agents	Glucose-Lowering_ Advantages
has_Cellular_mechanisms	Glucose-Lowering_Agents	Glucose-Lowering_ Cellular_mechanisms
has_Compounds	Glucose-Lowering_Agents	Glucose-Lowering_ Compounds
has_Cost	Glucose-Lowering_Agents	Glucose-Lowering_Cost
has_Disadvantages	Glucose-Lowering_Agents	Glucose-Lowering_ Disadvantages
has_Primary_physiological_ actions	Glucose-Lowering_Agents	Glucose-Lowering_Primary_ physiological_actions
has_History_of_Diseases	Patients	Glucose-Lowering_ Disadvantages
has_Adverse_Drug_Reactions	Patients	Glucose-Lowering_Agents
Not_recommand	Patients	Glucose-Lowering_Agents

Rule 1: *If patients have a history of diseases which are related to the disadvantages of glucose-lowering agents, then glucose-lowering agents are not recommended.*

Patients(?P) $\wedge$ has_History_of_Diseases(?P, ?S1) $\wedge$ Glucose-Lowering_Agents(?ND) $\wedge$ has_Disadvantages(?ND, ?S2) $\wedge$ sameAs(?S1, ?S2) $\rightarrow$ Not_recommand(?P, ?ND)

Rule 2: *If patients have Adverse Drug Reactions (ADRs), then the ADRs are not recommended.*

Patients(?P) $\wedge$ has_Adverse_Drug_Reactions(?P, ?ND) $\rightarrow$ Not_recommand(?P, ?ND)

For example, patient_1 has a history of "Bone fractures" and "Weight gain". One of Sulfonylureas' disadvantages is "Weight gain", one of Insulins' disadvantages is "Weight gain", while TZDs has both disadvantages, "Bone fractures" and "Weight gain". By rule 1, Sulfonylureas, Insulins and TZDs will not be recommended for patient_1. Patient_1 also has Adverse Drug Reactions (ADRs) to SGLT2. Thus, by rule 2, SGLT2 will not be recommended to patient_1.

5. **Experiments and Discussion.** The website of the drug recommendation system is: http://120.109.46.42/T2DMv1/. The endocrinologist created ten virtual patients' medical data to evaluate decision support system. The virtual patients' medical data, ideal *HbA1c* target and recommendation antidiabetic drugs are shown in Table 5. Then, the participants are evaluated of 8-question, 5-point survey, in terms of perceived usefulness, satisfaction degree, and behavioral intentions to use. The feedback given by the clinicians will be used for the maintenance of the ontology and the prototype.

The system was evaluated by an endocrinologist and an attending physician. The questionnaire evaluations have shown in Table 6. With regard to measuring the usefulness of the system, clinicians like to use the system and the system is recommended and the CDSS has good performance and is useful. The system also has over 80% of accuracy that can be used to assist clinicians at the management of diabetes mellitus during selecting drugs. As a result, 70% of clinicians will frequently use this system in the future due to the fact that the prescription strategy of clinical doctors must consider the other factors such as the price of drugs. In addition, the system has the following clinical values:

TABLE 5. Ten virtual patients' medical data

ID	age	sex	x_1, x_2, x_3, x_4, x_5, x_6, x_7	has_History of Diseases	has_ ADRs	z (*HbA1c* target)	Recommendation antidiabetic medications
01	73	female	3, 2, 3, NaN, NaN, NaN, NaN	increasing_LDL-C, Edema	GLP-1	8.6	Biguanides, DPP-4, Insulins, Sulfonylureas.
02	75	female	3, 2, 4, NaN, NaN, NaN, NaN	Heart_failure, increasing_LDL-C	Na	8.6	Biguanides, DPP-4, GLP-1, Insulins, Sulfonylureas.
03	64	female	2, 1, 2, NaN, NaN, NaN, NaN	Bone_fractures, increasing_LDL-C	Na	6.9	Biguanides, DPP-4, GLP-1, Insulins, Sulfonylureas.
04	76	female	4, 3, 3, 2, 1, NaN, NaN	increasing_LDL-C, Contraindications_ CKD	DPP-4	8.8	GLP-1, Insulins, Sulfonylureas.
05	61	female	4, 3, 2, 3, 2, NaN, NaN	Heart_failure, increasing_LDL-C, Contraindications_ CKD, Weight_gain	Na	8.6	GLP-1, DPP-4.
06	64	female	2, 1, 1, NaN, NaN, 2, NaN	Na	Na	6.9	Biguanides, SGLT2, DPP-4, GLP-1, TZDs, Sulfonylureas, Insulins.
07	62	male	2, 2, 3, NaN, NaN, 3, 1	Gastrointestinal_ side_effects_abdominal_cramping, increasing_LDL-C	Na	8.6	DPP-4, GLP-1, Insulins, Sulfonylureas.
08	81	female	4, 3, 4, 4, 4, 4, 2	MI, increasing_ LDL-C, Contraindications_CKD	DPP-4	8.6	GLP-1, Insulins, Sulfonylureas.
09	48	female	1, 1, 2, 3, NaN, NaN, 1	Patient_reluctance_ about_injection, increasing_LDL-C	Na	7.9	Biguanides, GLP-1, DPP-4, Sulfonylureas.
10	56	male	NaN, 2, 2, 2, 1, 1, NaN	Weight_gain, increasing_LDL-C, Gastrointestinal_ side_effects_nausea	TZDs	7.9	Biguanides, DPP-4.

(1) **Provide appropriate therapeutic goal and prescription and implement patient-centered medical care:**

Previous *HbA1c* control adopted leveled equality by down-adjusting the target levels. The patient-centered management strategy, it stresses individualized therapeutic goals. However, diabetes, multiple complications, and the complexity inherent in diabetes drug use often make it difficult for doctors, especially young doctors, to select the best therapeutic strategy. In view of this, we systematized the concept information to help doctors develop their therapeutic goal and prescriptions to meet the patient's needs. Therapeutic goals can thus achieve better.

TABLE 6. The questionnaire results of "A Patient-Centered Treatment Decision Support System for Diabetes" system

Question	Acceptance (%)
Do you think the system can provide some benefits for you?	
1. Using the system can improve my performance in my job.	4.5 (90%)
2. Using the system can enhance my effectiveness in my job.	4.0 (80%)
3. The system is useful in my job.	4.5 (90%)
What do you think about this system? Are you satisfied with its accuracy?	
1. Is the system accurate?	4.0 (80%)
2. Are you satisfied with the accuracy of the system?	4.0 (80%)
If this system is used in conjunction with the actual work, would you continue to use this system at work?	
1. I enjoy using this system at work.	4.0 (80%)
2. I will frequently use this system in the future	3.5 (70%)
3. I will strongly recommend to others to use this system.	4.0 (80%)

(2) **Save valuable time for both patients and doctors and make the best use of medical resources:**

The increasing number of patients exhausts medical resources. This system enables doctors to spend less time on medical diagnosis and adjustment of patients' prescriptions. This will reduce use of health care resources.

6. **Conclusions and Future Work.** The number of patients with diabetes is both large and increasing. Diabetes imposes psychological, physical, and financial hardship on patients. Thus, the prescription strategy of clinical doctors must consider many factors. To address this, we developed an individualized antidiabetic drug recommendation system for patients with diabetes. This system, which can be manipulated with relative ease, tailors *HbA1c* levels to satisfy the patient's individual differences. Currently, 13 kinds of glucose-lowering drugs, both oral and injected, are available. Taking all possible conditions into consideration is not only a waste of medical resources and a burden to the system, but is impractical. This study, which combines fuzzy logic and ontology reasoning, proposes a drug recommendation system for patients with diabetes. It promotes the new concept of "patient-centered diabetes therapy". In addition to aiding doctors' clinical diagnosis, the system can serve as a guide for specialty doctors. The system can also help non-specialty doctors and young doctors with their antidiabetic drug prescriptions. Based on the feedback system of operations, for example, the weight of seven factors can be dynamic to setting. We will improve our system interface and dynamic weighting calculations in the near future.

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REFERENCES

[1] International Diabetes Federation (IDF), *IDF Diabetes Atlas*, 7th Edition, Brussels, Belgium, 2015.
[2] R. Derr, E. Garrett, G. A. Stacy and C. D. Saudek, Is HbA1c affected by glycemic instability?, *Diabetes Care*, vol.26, no.10, pp.2728-2733, 2003.

[3] S. E. Inzucchi, R. M. Bergenstal, J. B. Buse, M. Diamant, E. Ferrannini, M. Nauck, A. L. Peters, A. Tsapas, R. Wender and D. R. Matthews, Management of hyperglycemia in type 2 diabetes, 2015: A patient-centered approach: Update to a position statement of the American diabetes association and the European association for the study of diabetes, *Diabetes Care*, vol.38, no.1, pp.140-149, 2015.

[4] American Diabetes Association, Standards of medical care in diabetes-2011, *Diabetes Care*, vol.34, no.Supplement 1, pp.S11-S61, 2011.

[5] Y. Handelsman, Z. T. Bloomgarden, G. Grunberger, G. Umpierrez, R. S. Zimmerman, T. S. Bailey, L. Blonde, G. A. Bray, A. J. Cohen, S. Dagogo-Jack, J. A. Davidson, D. Einhorn, O. P. Ganda, A. J. Garber, W. T. Garvey, R. R. Henry, I. B. Hirsch, E. S. Horton, D. L. Hurley, P. S. Jellinger, L. Jovanovič, H. E. Lebovitz, D. LeRoith, P. Levy, J. B. McGill, J. I. Mechanick, J. H. Mestman, E. S. Moghissi, E. A. Orzeck, R. Pessah-Pollack, P. D. Rosenblit, A. I. Vinik, K. Wyne and F. Zangeneh, American association of clinical endocrinologists and American college of endocrinology – Clinical practice guidelines for developing a diabetes mellitus comprehensive care plan – 2015, *Endocrine Practice*, vol.21, no.Supplement 1, pp.1-87, 2015.

[6] N. Guarino, D. Oberle and S. Staab, What is an ontology?, *Handbook on Ontologies*, Springer Berlin Heidelberg, Berlin, Heidelberg, 2009.

[7] C. Brewster and K. O'Hara, Knowledge representation with ontologies: Present challenges – Future possibilities, *International Journal of Human-Computer Studies*, vol.65, no.7, pp.563-568, 2007.

[8] P. Sharma and P. D. Kaur, Effectiveness of web-based social sensing in health information dissemination – A review, *Telematics and Informatics*, vol.34, no.1, pp.194-219, 2017.

[9] S. Fraihat, Ontology-concepts weighting for enhanced semantic classification of documents, *International Journal of Innovative Computing, Information and Control*, vol.12, no.2, pp.519-531, 2016.

[10] Y.-F. Zhang, Y. Tian, T.-S. Zhou, K. Araki and J.-S. Li, Integrating HL7 RIM and ontology for unified knowledge and data representation in clinical decision support systems, *Computer Methods and Programs in Biomedicine*, vol.123, pp.94-108, 2016.

[11] R. F. Alharbi, J. Berri and S. El-Masri, Ontology based clinical decision support system for diabetes diagnostic, *Science & Information Conference*, pp.597-602, 2015.

[12] D. E. Forbes, P. Wongthongtham, J. Singh and S. C. Thompson, Ontology supported assistive communications in healthcare, *Communications of the Association for Information Systems*, vol.34, pp.297-322, 2014.

[13] P. C. Sherimon and R. Krishnan, OntoDiabetic: An ontology-based clinical decision support system for diabetic patients, *Arabian Journal for Science and Engineering*, vol.41, no.3, pp.1145-1160, 2016.

[14] L. Marco-Ruiz, C. Pedrinaci, J. A. Maldonado, L. Panziera, R. Chen and J. G. Bellika, Publication, discovery and interoperability of clinical decision support systems: A linked data approach, *Journal of Biomedical Informatics*, vol.62, pp.243-264, 2016.

[15] A. B. Lugli, E. R. Neto, J. P. C. Henriques, M. D. A. Hervas, M. M. D. Santos and J. F. Justo, Industrial application control with fuzzy systems, *International Journal of Innovative Computing, Information and Control*, vol.12, no.2, pp.665-676, 2016.

[16] *Stanford Center for Biomedical Informatics Research (BMIR)*, http://protege.stanford.edu, Protégé, 2017.

[17] C.-T. Bau, R.-C. Chen and C.-Y. Huang, Construction of a clinical decision support system for undergoing surgery based on domain ontology and rules reasoning, *Telemedicine and e-Health*, vol.20, no.5, pp.460-472, 2014.

[18] R.-C. Chen, Y.-H. Huang, C.-T. Bau and S.-M. Chen, A recommendation system based on domain ontology and SWRL for anti-diabetic drugs selection, *Expert Systems with Applications*, vol.39, no.4, pp.3995-4006, 2012.

[19] R.-C. Chen, Y.-W. Lo, B.-Y. Liao and C.-T. Bau, Knowledge integration for diabetes drugs ontology, *Intelligent Data Analysis and Its Applications, Volume II: Advances in Intelligent Systems and Computing*, Springer International Publishing, 2014.

[20] S.-M. Chen, Y.-H. Huang, R.-C. Chen, S.-W. Yang and T.-W. Sheu, Using fuzzy reasoning techniques and the domain ontology for anti-diabetic drugs recommendation, *Asian Conference on Intelligent Information & Database Systems, Lecture Notes in Computer Science*, pp.125-135, 2012.

[21] A. S. Ellouze, R. Bouaziz and H. Ghorbel, Integrating semantic dimension into openEHR archetypes for the management of cerebral palsy electronic medical records, *Journal of Biomedical Informatics*, vol.63, pp.307-324, 2016.

[22] P. J. O'Connor, J. M. Sperl-Hillen, C. J. Fazio, B. M. Averbeck, B. H. Rank and K. L. Margolis, Outpatient diabetes clinical decision support: Current status and future directions, *Diabetic Medicine*, vol.33, no.6, pp.734-741, 2016.

[23] B. M. Scirica, D. L. Bhatt, E. Braunwald, P. G. Steg, J. Davidson, B. Hirshberg, P. Ohman, R. Frederich, S. D. Wiviott, E. B. Hoffman, M. A. Cavender, J. A. Udell, N. R. Desai, O. Mosenzon, D. K. McGuire, K. K. Ray, L. A. Leiter and I. Raz, Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus, *New England Journal of Medicine*, vol.369, no.14, pp.1317-1326, 2013.

[24] F. M. Turnbull, C. Abraira, R. J. Anderson, R. P. Byington, J. P. Chalmers, W. C. Duckworth, G. W. Evans, H. C. Gerstein, R. R. Holman, T. E. Moritz, B. C. Neal, T. Ninomiya, A. A. Patel, S. K. Paul, F. Travert and M. Woodward, Intensive glucose control and macrovascular outcomes in type 2 diabetes, *Diabetologia*, vol.52, no.11, pp.2288-2298, 2009.

[25] W. B. White, C. P. Cannon, S. R. Heller, S. E. Nissen, R. M. Bergenstal, G. L. Bakris, A. T. Perez, P. R. Fleck, C. R. Mehta, S. Kupfer, C. Wilson, W. C. Cushman and F. Zannad, Alogliptin after acute coronary syndrome in patients with type 2 diabetes, *New England Journal of Medicine*, vol.369, no.14, pp.1327-1335, 2013.

[26] A. Ceriello, M. Gallo, R. Candido, A. De Micheli, K. Esposito, S. Gentile and G. Medea, Personalized therapy algorithms for type 2 diabetes: A phenotype-based approach, *Pharmacogenomics and Personalized Medicine*, vol.7, pp.129-136, 2014.

[27] F. J. Ampudia-Blasco, P. Y. Benhamou, G. Charpentier, A. Consoli, M. Diamant, B. Gallwitz, K. Khunti, C. Mathieu, M. Ridderstråle, J. Seufert, C. Tack, T. Vilsbøll, T.-M. Phan and H. Stoevelaar, A decision support tool for appropriate glucose-lowering therapy in patients with type 2 diabetes, *Diabetes Technology & Therapeutics*, vol.17, no.3, pp.194-202, 2014.

[28] Sandia National Laboratories, *Jess*, http://www.jessrules.com/, 2017.