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An ontology-driven clinical decision support system (IDDAP) for infectious disease diagnosis and antibiotic prescription

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ABSTRACT

Background: The available antibiotic decision-making systems were developed from a physician's perspective. However, because infectious diseases are common, many patients desire access to knowledge via a search engine. Although the use of antibiotics should, in principle, be subject to a doctor's advice, many patients take them without authorization, and some people cannot easily or rapidly consult a doctor. In such cases, a reliable antibiotic prescription support system is needed.

Methods and results: This study describes the construction and optimization of the sensitivity and specificity of a decision support system named IDDAP, which is based on ontologies for infectious disease diagnosis and antibiotic therapy. The ontology for this system was constructed by collecting existing ontologies associated with infectious diseases, syndromes, bacteria and drugs into the ontology's hierarchical conceptual schema. First, IDDAP identifies a potential infectious disease based on a patient's self-described disease state. Then, the system searches for and proposes an appropriate antibiotic therapy specifically adapted to the patient based on factors such as the patient's body temperature, infection sites, symptoms/signs, complications, antibacterial spectrum, contraindications, drug–drug interactions between the proposed therapy and previously prescribed medication, and the route of therapy administration.

The constructed domain ontology contains 1,267,004 classes, 7,608,725 axioms, and 1,266,993 members of "SubClassOf" that pertain to infectious diseases, bacteria, syndromes, anti-bacterial drugs and other relevant components. The system includes 507 infectious diseases and their therapy methods in combination with 332 different infection sites, 936 relevant symptoms of the digestive, reproductive, neurological and other systems, 371 types of complications, 838,407 types of bacteria, 341 types of antibiotics, 1504 pairs of reaction rates (antibacterial spectrum) between antibiotics and bacteria, 431 pairs of drug interaction relationships and 86 pairs of antibiotic-specific population contraindicated relationships.

Compared with the existing infectious disease-relevant ontologies in the field of knowledge comprehension, this ontology is more complete. Analysis of IDDAP's performance in terms of classifiers based on receiver operating characteristic (ROC) curve results (89.91%) revealed IDDAP's advantages when combined with our ontology.

Conclusions and significance: This study attempted to bridge the patient/caregiver gap by building a sophisticated application that uses artificial intelligence and machine learning computational techniques to perform data-driven decision-making at the point of primary care. The first level of decision-making is conducted by the IDDAP and provides the patient with a first-line therapy. Patients can then make a subjective judgment, and if any questions arise, should consult a physician for subsequent decisions, particularly in complicated cases or in cases in which the necessary information is not yet available in the knowledge base.

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1. Introduction

Infection constitutes the invasion of an organism's body tissues by disease-causing agents, the multiplication of these agents, the

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reaction of host tissues to these organisms and the toxins produced by these organisms [1]. Approximately 20% to 40% of hospital patients with infections are treated with antibiotics, and the associated costs account for at least 25% of the pharmacy department's budget [2].

In the field of medicine, clinicians cannot obtain the necessary knowledge regarding clinical processes from the currently inadequate medical databases. The abundance of inappropriate quotations constitutes noise and requires a tedious sorting process that is incompatible with the practice of medicine [3]. To address this problem, many studies have investigated processing knowledge bases with a decision-support system (DSS) [4], which is a probabilistic and quantitative method used to model problems in situations that involve ambiguity.

One of the first DSSs developed for antibiotic therapy was Health Evaluation through Logical Processing (HELP) [5], an integrated hospital information system that combines both communication and advice functionality. The system is based on the use of different knowledge frames, which are modules that allow the system to react when new patient data are introduced. These reactions include the generation of alarms, reminders, diagnostic suggestions and therapeutic recommendations [6]. Some particular DSSs for antibiotic therapy that have been developed inside the HELP environment focus on improving antibiotic therapy for microbiologically confirmed infections [7], for antibiotic surgical prophylaxis [8] and for empirical antibiotic therapy [9]. The observed clinical effects from these DDSs include a significant improvement in antibiotic surgical prophylaxis, progressive changes in therapy prescriptions by physicians due to alerts generated by the DSSs, and a decreased rate of antibiotic-associated adverse events.

Another expert system [10] was developed in North Carolina Baptist Hospital with the aim of improving anti-microbial therapy. This expert system simultaneously examined data regarding patient demographics, culture results, associated susceptibility test results, cutoff values for susceptibility and anti-microbial therapies downloaded from various databases. This expert system has four potential problems: (1) no therapy is identified despite the presence of pathogens, (2) the implemented therapy is ineffective against the isolated pathogens, (3) the therapy cannot be matched to the susceptibility data of the isolated pathogens, or (4) the therapy is rapidly discontinued.

Another system [11] targeted the important decision points that arise in first-day management of patients who are suspected, or known, to have a bacterial infection. This system uses causal probabilistic networks to calculate the probability distributions for the relevant output variables and uses decision theory to balance the therapeutic benefit of antibiotic therapy against the detriments associated with antibiotic drugs.

In addition, many studies have investigated the use of ontologies in DSS and disease diagnosis. Natural language applications are limited due to their lack of formality and their non-collective interpretations. In contrast, ontologies [12] can capture the intended meaning and specify modeling primitives. Ontologies are knowledge representations using controlled vocabularies that are designed to help knowledge sharing and computer reasoning [13]. Recently, ontologies have gained increasing relevance in the biomedical domain because they enable researchers to stay abreast of current biomedical knowledge and promote the understanding of such information.

Köhler et al. [14] presented a method for clinical diagnostics based on a newly developed ontological search routine that uses the semantic structure of the Human Phenotype Ontology (HPO) to weigh clinical features based on specificity and to identify those clinical features that best represent the top candidate differential diagnoses. Bauer et al. [15] developed the Bayesian Ontology Query

Algorithm (BOQA), which integrates the knowledge stored in an ontology and the accompanying annotations into a Bayesian network to implement a search system in which users enter one or more terms from the ontology to obtain a list of the best-matching domain items. These two studies focused on researching semantic similarity searches based on ontologies and proved very instructive. However, because the process of infectious disease diagnosis mainly involves a filtering procedure [4], the probability calculation methods proposed by these two studies are appropriate for the diagnosis of diseases other than infectious diseases.

The available antibiotic decision-making systems were developed from a physician's perspective. However, because infectious diseases are common, many patients desire access to knowledge via a search engine. There are high risks associated with the use of antibiotics without prior consultation with a physician. Although the use of antibiotics should, in principle, be subject to a doctor's advice, many patients take them without authorization, and many individuals cannot easily or quickly consult a doctor. In such cases, a reliable antibiotic prescription support system is needed. Physicians in different settings, such as private clinics, community health centers, and nursing homes, have different therapy capacities in terms of available time and expertise. These clinical settings would save time by having a decision-making system that incorporates patient symptoms [16]. Therefore, this study aimed to provide a method that creates a DSS (IDDAP) for infectious diseases using patient-entered and patient-reported information. The proposed IDDAP screens for an appropriate therapy and proposes an antibiotic therapy specifically adapted to the patient. The first level of the decision-making process is completed by the computer; then, patients can make a subjective judgment. If any questions arise, subsequent decisions should be made by a physician. Physicians are involved in an IDDAP in several ways, including detailing the relationships between microorganisms, body sites, and infections and aiding system developers in IDDAP's development and evaluation.

Here, we implement an IDDAP for the infectious disease domain by automatically collecting behavior clusters and automatically generating ontologies. The research emphasis mainly includes the following: 1) constructing and enriching an ontology [S1 ontology file], 2) designing and using a system that incorporates a patient's self-inspection concerning infectious diseases [S2 software and S3 video], 3) identifying and categorizing possible infectious diseases using knowledge structured by an ontology [S2 software and S3 video], and 4) evaluating the proposed IDDAP and ontology [S4 classification results]. IDDAP uses a first-cut metric to assess its validity, which is largely an assessment of its technical rather than its medical validity. This metric evaluates the knowledge comprehensiveness of the generated ontology, assesses IDDAP's classification performance, and surveys the understanding of IDDAP from a patient's perspective. In future work, other validity metrics will be considered.

2. Materials and methods

2.1. Ontologies

In this study, IDDAP's operation for infectious diseases is based on ontologies, which are proposed for the axiomatization of knowledge domains. Compilation of an ontology requires an abundance of data sources. With the exception of medical records provided by doctors, many infection disease-relevant ontology resources were adopted to construct the infectious disease diagnosis ontology. These ontology resources have played useful roles in facilitating the re-use, dissemination and sharing of patient information across disparate platforms.

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