A Knowledge-based Clinical Decision Support System for Headache Disorders Management

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Abstract: Headache is one of the most common neurological problems faced by General Practitioners (GPs) and neurologists. Most of GPs find the diagnosis of headache rather difficult: paper-based guidelines are long and the diagnostic criteria are complex. Thus, many headache patients do not have an early accurate diagnosis of headaches' type and an appropriate treatment. In order to overcome this burden, we present a knowledge-based Clinical Decision Support System (CDSS) specifically devoted to support GPs in the headache diagnosis and in the appropriate selection of the diagnostic-therapeutic path. The proposed CDSS has been designed and developed based on internationally validated guidelines and clinical protocols. The knowledge base contains the medical-clinical knowledge appropriately formalized in several set of rules. Communication interfaces compliant with HL7 DSS (Health Level Seven Decision Support Service) international standard were developed enabling interoperation with other healthcare applications. The CDSS has been tested and assessed in the GPs' daily practice of the Calabria Cephalalgic Network. During the evaluation period, a reduced number of requests for neurological visits and unnecessary and expensive instrumental examinations was registered. The results obtained from the evaluation period demonstrate that the CDSS turns out to be effective in the management of headache patients.

1 INTRODUCTION

Headache disorders represent a worldwide problem, affecting people of all ages, races and geographical areas (World-Health-Organization, 2016). In Italy, according to a survey by National Institute of Statistics, the recurrent headache is one of the chronic diseases with higher incidence. It is fourth after arthritis, arterial hypertension and allergic diseases (Istat, 2015). Notwithstanding, many patients with chronic headaches do not receive effective treatment, mainly due to the underestimation of the impact of the disease and to the complexity of diagnostic criteria (World-Health-Organization, 2016). As a negative consequence, headache attacks are very often self-managed by patients that progressively increase the assumption of analgesics until they reach a condition of medication-overuse (Elkind, 1991).

The General Practitioner (GP) has a central role in the headache diagnosis process as the GP has the first contact with the patient making a first diagnosis. The GP can effectively treat the majority of patients with headache disorders; only a minor group requires higher medical specializations as a neurologist or advanced instrumental examinations (Steiner et al., 2007). For this reason, it is strategically important that the GP be able to make an accurate diagnosis and therefore has a deep knowledge of the diagnostic criteria. In this way, patients can immediately get an effective treatment, reduce pain and discomfort.

A Clinical Decision Support System (CDSS) could get a great advantage over paper-based protocols and guidelines. Paper-based guidelines to support headache diagnosis are typically long and difficult to memorize or refer during patient interviews. A CDSS instead, has many advantages because it can: (1) assists the GP for an accurate symptoms' detection; (2) provide an accurate support in processing a large number of data, and (3) offer a level of speci-

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ficity for individual patient that is nearly hard to get by using a paper-based guideline.

In this paper, we design, develop, and evaluate a knowledge-based CDSS able to support the GP both in the headache diagnosis and the choice of best diagnostic-therapeutic path according to patient's symptoms. The CDSS uses a rule-based approach. It has been designed and developed based on internationally validated guidelines and clinical protocols. Communication interfaces compliant with HL7 DSS (Health Level Seven Decision Support Service) international standard were developed in order to enable the interoperation with other healthcare applications. Results from the evaluation of the CDSS in the management of the Calabria Cephalalgic Network clinical workflow are presented.

The paper is organized as follows. Section 2 introduces the background on headache disorders and the main works on CDSSs. Section 3 presents the Calabria Cephalalgic Network healthcare context. Section 4 describes the proposed CDSS. Section 5 presents results and a brief discussion. Finally, Section 6 concludes the paper.

2 BACKGROUND

As reported in the International Classification of Headache Disorders (ICHD) published by the International Headache Society (IHS) (IHS, 2018), there are three main categories of headache disorders: primary headaches; secondary headaches and painful cranial neuropathies; other facial pains and other headaches. Each category is divided into sub-categories. The three major primary headache sub-categories are migraine (with and without aura), tension-type headache, and cluster headache. Secondary headaches are due to other disorders (the so-called comorbidities) such as infections or traumas cranium. In addition, a secondary headache can be attributed to a substance or its withdrawal, e.g. medication-overuse headache. In severe cases, a headache is often an initial warning symptom of serious diseases such as an ischaemic or haemorrhagic stroke. In these cases, headaches appear along with other warning symptoms.

In the literature, several tools have already been proposed and developed to support health professionals in the diagnosis of headache disorders (Potter et al., 2018; Aljaaf et al., 2018). Some tools have been developed to classify only one type of headache. For instance, the CDSS presented in (Kopec et al., 2004) is a rule-based expert system that supports clinicians to migraine diagnosis. The rules are represented in the C Language Integrated Production System. Other tools support clinicians in the diagnosis of multiple headache types. The CDSS developed in (Yin et al., 2015) is specialized to diagnose migraine and tension-type headaches. It is based on case-based reasoning. Previous solved cases are stored in a built-in library, and a k-nearest neighbour algorithm is used to measure similarity among cases. More complex is the hybrid system based on both rules and case-based reasoning in (Yin et al., 2014). This system is useful to diagnose the main primary headaches, i.e., migraine, tension-type headache, and cluster headache: First, patients' symptoms are evaluated in a rule-based module and only if a diagnosis cannot be suggest, the system searches for the most similar previous case in a case-based module. Migraine and other secondary headache diseases can be diagnosed by the CDSS in (Zafar et al., 2013). An image processing module is also included to detect brain tumour from MRI scans. A knowledge-based system that uses yes/no questions derived from neurology experts is the CDSS in (Hasan et al., 2012). More specifically, neurologist's knowledge has been converted in a tree diagram.

Guideline-based systems are presented in (Simić et al., 2008; Eslami et al., 2013; Dong et al., 2014). The second version of ICHD criteria were codified in the CDSS of (Eslami et al., 2013) to classify the main types of primary headaches (i.e., migraine, tension-type headache and cluster headache). This CDSS proposes a questionnaire to patients and implements a simple human-like algorithmic reasoning. The same version of ICHD criteria were also codified in (Simić et al., 2008); the difference is that the developed CDSS uses a fuzzy logic as implementation technology. The third version of ICHD criteria were implemented in the CDSS in (Dong et al., 2014): clinicians are assisted to diagnose primary headache disorders and medication-overuse headaches.

The CDSSs developed in (Krawczyk et al., 2013; Çelik et al., 2015; Keight et al., 2017) are on machine learning techniques based. In (Krawczyk et al., 2013), the authors defined the diagnosis of primary headache as a classification task. They compared three feature selection techniques and several classifiers on the same set of patients. In (Keight et al., 2017) nine machine learning based classifiers are compared on a dataset consisting of primary headaches, and the best predictive performance was achieved by a stacking classifier. In (Çelik et al., 2015) Artificial Immune Systems were used as classification algorithms to diagnose migraine, tension-type headache, and cluster headaches. A further extension of this work evalu-

ates an ant-colony optimization algorithm on the same dataset (Celik and Yurtay, 2017).

The CDSS in (Vandewiele et al., 2018) is one of the most recent systems for the diagnosis and classification of the headache disorders. It implements an automated diagnosis support module that generates an interpretable decision tree based on data semantically annotated with expert knowledge.

To summarize, the analysed systems use different sources of knowledge, architecture and implementation technology to diagnose headaches. Nevertheless, these tools support clinicians in headache diagnosis but not in patient management after a diagnosis. As a result, in many cases GPs refer patients to headache specialists for unnecessary examinations.

To the best of our knowledge, there are currently no systems allowing complete screening of headaches, that is, primary headache, secondary headache, and warning symptoms in primary care.

3 CALABRIA CEPHALALGIC NETWORK: INNOVATION IN THE CLINICAL WORKFLOW MANAGEMENT

The Calabria Cephalalgic Network represents a novel healthcare delivery context. It has been designed in Calabria (Italy) and it is based on a patient-centred integrated approach. Its main objective concerns the management of headache patients through personalized care pathways, ensuring continuity of care at different levels of diagnostic-therapeutic paths.

The architectural organization of the network is reported in Figure 1. The network is organized in three levels: GPs, Spokes and Reference Centres. All the levels interact with Emergency Department.

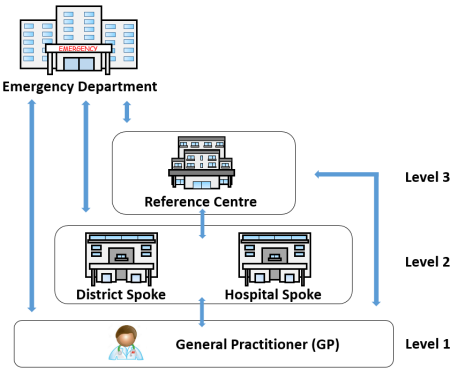

Figure 1: Organization of Calabria Cephalalgic Network.

GPs are in the first level. They represent the core node of the network since they have the first contact with patients. GPs acquire patient's signs and symptoms through clinical interviews and refer the patient to the most appropriate diagnostic-therapeutic path. In case of diagnostic uncertainty and/or ineffectiveness of the prescribed therapy, the GPs interact with the second level; in more complex situations, such as for instance, headache with aura, serious comorbidities, cluster headaches, and medication-overuse headaches, the GPs interact with the third level.

District Spoke and Hospital Spoke are in the second level. The District Spoke manages patients needing specialized clinical assessments, whereas the Hospital Spoke manages patients needing deeper assessments based on instrumental investigations.

The Reference Centre is the third level. It mainly manages patients with comorbidities, headaches with aura focusing on rehabilitation of patients with medication-overuse headaches. Moreover, it manages patients with cluster headaches and coming from Spoke with diagnostic uncertainty.

It is important to remark that, at each level, health professionals follow evidence based specific guidelines for patient care, facilitating the coordination with other health professionals.

Figure 2 shows the GPs' clinical workflow in the Calabria Cephalalgic Network.

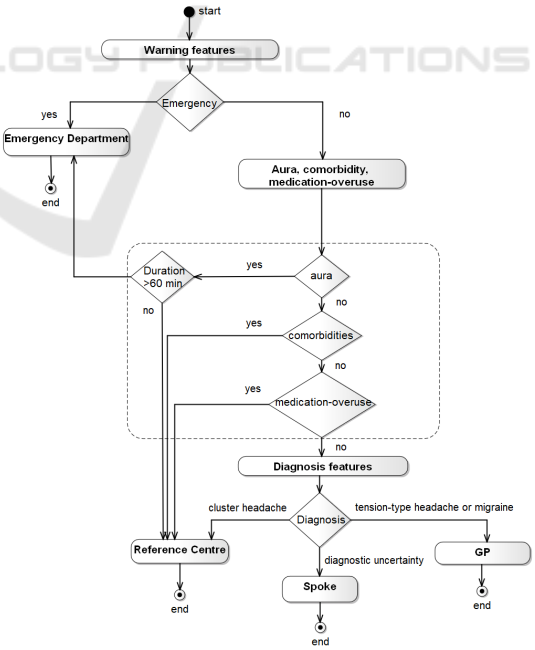

Figure 2: Clinical workflow for the GPs in the Calabria Cephalalgic Network.

The GPs' clinical workflow can be summarised as follows. At the baseline visit, a GP has to immediately assess possible emergency conditions. In case of warning symptoms, the GP refers the patient to the Emergency Department. Otherwise, the clinical investigation continues and the GP assesses aura symptoms. If each individual aura symptom lasts less than 60 minutes, the patient should be referred to the Reference Centre; otherwise, to the Emergency Department. If there are not aura symptoms, the GP assesses comorbidities and medication-overuse: serious comorbidities or medication-overuse headaches prompt the GP to refer the patient to the Reference Centre. The GP will be able to identify primary headache subtypes only if all of the health conditions described so far have been ruled out: patients with cluster headaches should be referred to the Reference Centre; patients in case of diagnostic uncertainty should be referred to the Spoke; with diagnosis of migraine or tension-type headache are treated by the GP.

4 CDSS DESIGN AND DEVELOPMENT

The CDSS was designed to support GPs in the diagnosis and choices of therapeutic paths in a primary care context. It is fully compliant with clinical guidelines and diagnostic-therapeutic paths applied within the Calabria Cephalalgic Network.

The development of the CDSS followed an iterative approach involving engineers, GPs and neurological specialists who collaborated to identify functional requirements. First, the guideline recommendations were combined with expert knowledge to determine system responses based on patient data. Then, the communication interfaces of the system were developed.

The general architecture of the proposed CDSS is reported in Figure 3. The CDSS consists of three main components: knowledge base, inference engine and CDSS interface. Communication interface and GUI (Graphical User Interface) complete the architecture of the system. The CDSS was designed to work in a collaborative environment. According to this vision, a user is any external entity that interacts with the CDSS such as a GUI, another CDSS, an electronic medical record or any other component and service of the health environment.

The three main components of the CDSS, the communication interface and GUI are described in the next sections. The CDSS interface receives and validates the patient data contained in each request. If the data is correct, it activates the inference engine.

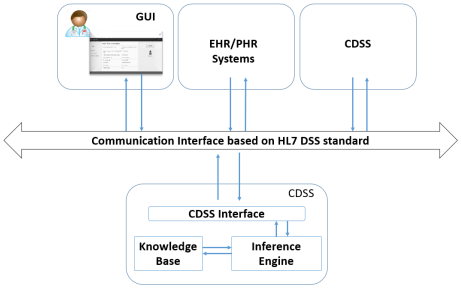

Figure 3: CDSS Architecture.

4.1 Knowledge Base

The knowledge base contains the medical-clinical knowledge appropriately formalized by the relevant sets of rules. The National Institute for Health and Care Excellence (NICE) Clinical Guideline for headache disorders (Carville et al., 2012), the workflow of the GPs and health professionals' experiences in the Calabria Cephalalgic Network, were appropriately coded as sources of knowledge.

The clinicians' expertise and their suggestions have been obtained through various interviews with both GPs and neurologists.

All rules were coded as IF-THEN statements in the Java programming language.

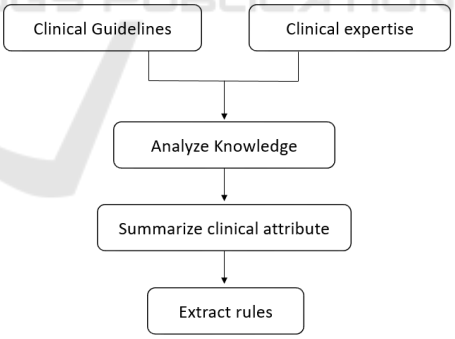

Figure 4: Knowledge Acquisition Process.

Figure 4 summarizes the adopted process of knowledge acquisition for the headache disorders diagnosis. First, knowledge from different sources have been acquired, analysed and expressed in several flowcharts. Each flowchart has been validated by clinicians. Then, headache clinical attributes have been defined and summarized. The acquired knowledge has been translated in a set of conditional rules.

According to the diagnostic and therapeutic paths of the Calabria Cephalalgic Network, five sets of rules have been codified for the diagnosis of headache

disorders such as primary headaches (migraine, tension type and cluster headache), warning symptoms, aura's symptoms, comorbidities, medication-overuse headaches. Rules for the management of the patient's therapeutic path have also been coded. Table 1 reports the headache features used to create the diagnostic rules. Table 2 reports one rule for cluster headache diagnosis.

Each headache clinical attribute is designed as categorical and identifies the allowed values. Table 3 lists the primary headache categorical attributes.

Table 1: Headache features used to create the diagnostic rules.

Diagnosis	Features
Warning events	Headache that begins after age 50
	Headaches increasing in frequency, duration and severity
	Headache subsequent to head trauma in the previous 3 months
	Unusual headache accompanied by fever and rigor nucalis
	Headache with physical exertion (coughing, sneezing)
	Paresthesia of lower limb
	Anticoagulant therapy
	Limb strength deficit
	Sensory deficits
	Disorders of consciousness
	Speech disorders
	Visual disturbances
	Disorders of vigilance
Aura, Comorbidity, Medication-overuse	Flashes of light
	Lines
	Scotomas or spots
	Aura duration
	Paresthesia
	Language disorders
	Regular overuse for > 3 months of one or more drugs
	Endocrine and metabolic disorders
	Cardiovascular disease
	Psychiatric disorders
	Severe hypertension
Primary headache	Pain Location
	Pain Quality
	Pain Intensity
	Effect on activities
	Duration of headache
	Frequency of headache
	Red eye
	Watery eye
	Nasal congestion
	Runny nose
	Swollen eyelid
	Forehead and facial sweating
	Constricted pupil
	Drooping eyelid
	Vomiting
	Nausea
	Photophobia
	Phonophobia

Table 2: One rule for cluster headache diagnosis.

Rule Name	Rule Condition
Rule 1	IF (Criterion 1 AND Criterion 2 AND Criterion 3 AND Criterion 4 AND Criterion 5 AND Criterion 6 AND Criterion 7) THEN Cluster Headache
Criterion 1	IF (Pain Location=Unilateral) THEN true
Criterion 2	IF (Pain Quality=Variable) THEN true
Criterion 3	IF (Pain Intensity=Severe OR Pain Intensity=Very severe) THEN true
Criterion 4	IF (Effect on activities=Restlessness OR Effect on activities=Agitation) THEN true
Criterion 5	IF (Other symptoms=Red eye OR Other symptoms=Watery eye OR Other symptoms=Nasal congestion OR Other symptoms=Runny nose OR Other symptoms=Swollen eyelid OR Other symptoms=Forehead and facial sweating OR Other symptoms=Constricted pupil OR Other symptoms=Drooping eyelid) THEN true
Criterion 6	IF (Duration of headache= 15-180 minutes) THEN true
Criterion 7	IF (Frequency of headache= 1 every other day to 8 per day) THEN true

4.2 Inference Engine

The inference engine receives and manages all the requests coming via the CDSS interface. Based on the input patient data, it identifies and activates specific sets of rules for obtaining a decision support, as illustrated in Figure 5. It firstly searches for all the possible rules that match with the patient input data in the knowledge base. Then, the execution of the selected

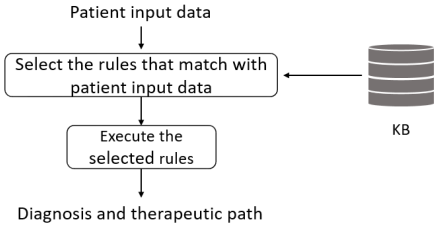

Figure 5: Workflow of the Inference Engine.

rules starts. It returns the patient-specific diagnosis and therapeutic path on the basis of satisfied rules.

4.3 Communication Interface

The CDSS communication interface was developed as SOAP web service compliant with the HL7 DSS international standard (HL7DSS, 2017). It defines a standard interface for decision support applications, regardless of data format, inference mechanisms and implementation technology. The HL7 DSS standard guarantees the interoperability of the CDSS with other applications in the healthcare environment.

Table 3: Primary headache categorical values.

Variable	Allowed values
Pain Location	Bilateral, Unilateral, Mono/Bilateral
Pain Quality	Pulsating, Variable, Pressing/tightening (non-pulsating)
Pain Intensity	Mild, Moderate, Severe, Very severe
Effect on activities	Not aggravated by routine activities, Aggravated by routine activities, Restlessness, Agitation
Other symptoms	Photophobia, Phonophobia, Nausea, Vomiting, Red eye, Watery eye, Nasal congestion, Runny nose, Swollen eyelid, Forehead and facial sweating, Constricted pupil, Drooping eyelid
Duration of headache	30 minutes-continuous, 4-72 hours, 15-180 minutes
Frequency of headache	< 15 days per month, > 15 days per month, 1 every other day to 8 per day

4.4 Graphical User Interface

The GUI has three main parts including warning symptoms questions page, aura, comorbidity and medication-overuse symptoms question page, primary headache symptoms question page. A decision page where patient-specific diagnosis and therapeutic path are explained, have been implemented. The first diagnostic web page is the warning symptoms question page. The GP inserts patient data in appropriate fields. The data are thus evaluated by the CDSS. If no alert is detected, the GP can continue the diagnostic process and the second question page is shown; otherwise, the decision page is presented with the patient-specific diagnostic path. The second diagnostic page concerns aura, comorbidity and medication-overuse symptoms question page. The GP fills in the fields with patients' clinical characteristics, which are evaluated by the CDSS. If no clinical condition is detected, the GP can continue the diagnostic process. The third page is the primary headache symptoms question page. After the evaluation of the CDSS, the final decision page is presented to the GP. Figure 6 shows the three diagnostic steps. The web pages are

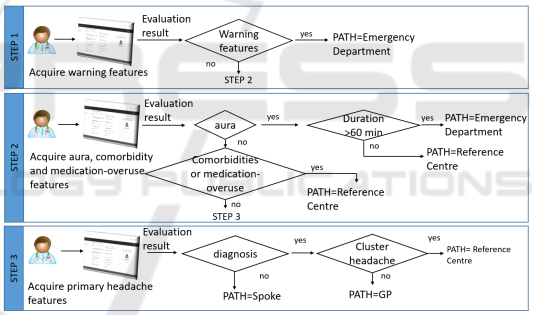

Figure 6: Diagnostic steps.

both Italian and English language. Figure 7 shows the primary headache symptoms question page.

4.5 Functional Specifications

When a patient assessment is required, the GP sends a request message to the CDSS, via GUI, to activate the clinical decision support. The requested data are forwarded to the inference engine through the CDSS's interface. The inference engine, based on the submitted data, identifies the more appropriate rules set in the knowledge base and performs it. The CDSS returns the diagnostic and the patient care path suggestions to the GUI.

The proposed CDSS is a plug and play system based on the Service Oriented Architecture paradigm (Erl, 2005); it has been modelled following the Model Driven Architecture methodology (MDA, 2012).

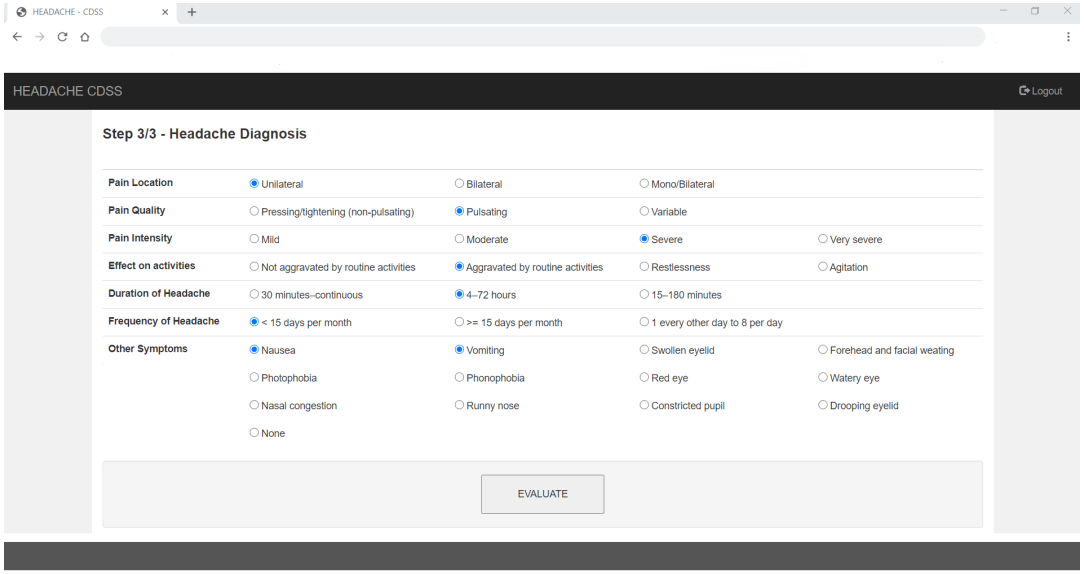

Figure 7: GUI for the diagnosis of primary headache type.

As regards privacy and data protection, the CDSS does not use patient identification data and bidirectional communication data is encrypted.

5 RESULTS AND DISCUSSION

To investigate the performance of the proposed CDSS, we firstly performed an assessment of the system on available datasets. In order to measure the effectiveness of the proposed CDSS in the primary headache diagnosis, we used a publicly available dataset hosted on http://www.migbase.com/migbase_dataset.xls. The dataset contains answers to questionnaires of 850 patients with headache problems. A neurologist labelled each sample in migraine, tension-type headache, and cluster headache; only one sample has been labelled as no headache. The proposed CDSS correctly recognized 609/609 (100%) patients with migraine, 155/184 (84.23%) patients with tension-type headache, and 55/56 (98.21%) patients with cluster headache. Overall, the CDSS correctly recognized 816 (96%) patients; suggested diagnostic uncertainty and further clinical investigation for 25 (2.94%) patients, whereas only 9 (1.06%) patients were misclassified. Because no real data was available, we produced realistic test data for different types of secondary headaches and warning symptoms. Although the use of real data was clearly preferable, the use of this data allowed us to test all rule sets implemented under the supervision of a clinical expert. The dataset consists of 10 cases. The CDSS classified correctly all the cases.

We further explored the use of the CDSS in a real healthcare setting. The CDSS has been deployed in the Calabria Cephalalgic Network and experimentally evaluated in daily practice by the GPs during a period of 5 months. The real case study involved 10 GPs, 1 Reference Centre, 3 Spokes, and 80 patients. Before the practical evaluation, the CDSS was presented at GPs during several training events. The GPs were interviewed during the evaluation period and at the end, in order to judge the performance of the CDSS and its impact in a daily practice. Interviews were also conducted with the Spoke and the Reference Centre to evaluate how neurologists and GPs managed patients. GPs considered the CDSS useful and were satisfied by its performance: the CDSS is easy to use, patients data is collected in a short time, the given support in diagnosis is fundamental especially for complex cases. Compared to the previous 5 months, the neurologists of the Reference Centre recorded a reduction of accesses for episodic migraine diagnosis during the evaluation period, i.e., 12.5% vs 5%. This result suggests an improvement in management of patients with headache for the GP and therefore, a reduced demand for unnecessary and expensive instrumental examinations. The proposed CDSS really supports GPs to manage patients with headaches. As a consequence, a more appropriate use of healthcare resources there is.

6 CONCLUSIONS

This paper has presented a knowledge-based CDSS to support GPs for the integrated clinical management

of headache patients. The knowledge base codes the NICE Clinical Guideline for headache disorders, the GP clinical workflow and the clinical best practices from the Calabria Cephalalgic Network. Communication interfaces are compliant with HL7 DSS international standard in order to guarantee interoperability with other healthcare applications.

The CDSS has been assessed in the GPs' daily practice of the Calabria Cephalalgic Network. The preliminary results are promising. They confirm an improvement in the management of patients with headache within primary care facilities. The CDSS effectively supports GPs in dealing with a patients headache diagnosis by reducing diagnosis time on the one hand, even during the anamnesis phase, inappropriate accesses to the Spokes and Reference Centre, and patient's expenses on the other hand for headache treatments.

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