A logic-based decision support system for the diagnosis of headache disorders according to the ICHD-3 international classification

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Abstract

Decision support systems play an important role in medical fields as they can augment clinicians to deal more efficiently and effectively with complex decision-making processes. In the diagnosis of headache disorders, however, existing approaches and tools are still not optimal. On the one hand, to support the diagnosis of this complex and vast spectrum of disorders, the International Headache Society released in 1988 the International Classification of Headache Disorders (ICHD), now in its 3rd edition: a 200 pages document classifying more than 300 different kinds of headaches, where each is identified via a collection of specific nontrivial diagnostic criteria. On the other hand, the high number of headache disorders and their complex criteria make the medical history process inaccurate and not exhaustive both for clinicians and existing automatic tools. To fill this gap, we present HEAD-ASP, a novel decision support system for the diagnosis of headache disorders. Through a REST Web Service, HEAD-ASP implements a dynamic questionnaire that complies with ICHD-3 by exploiting two logical modules to reach a complete diagnosis while trying to minimize the total number of questions being posed to patients. Finally, HEAD-ASP is freely available on-line and it is receiving very positive feedback from the group of neurologists that is testing it.

KEYWORDS: Knowledge Representation, ASP, Artificial Intelligence, ICHD-3

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1 Introduction

1.1 Context and state-of-the-art

Decision support systems (DSS) have been conceived for providing the “information and analysis necessary for the decisions that must be made” (Donovan 1976). After almost 50 years, DSSs are still evolving, and they play an important role in various application domains. For example, they can augment clinicians to deal more efficiently and effectively with complex decision-making processes such as diagnostics, disease management, and drug control (Sutton et al. 2020). Since the seventies, most has been done both in medicine and computer science to make DSS more and more robust and reliable. But in some specific fields, such as the diagnosis of headache disorders, existing approaches and tools are still not optimal.

Headache disorders represent one of the most common and disabling conditions of the nervous system throughout the world (Stovner et al. 2007). In particular, about 90% of all headaches are primary, namely, magnetic resonance imaging of the brain reveals no abnormality (Evans 2017). To support the diagnosis of this complex and vast spectrum of disorders, in 1988, the International Headache Society (2018) released the first edition of the International Classification of Headache Disorders (ICHD), now in its 3rd edition: a document of 200 pages classifying, in a taxonomic way, more than 300 different kinds of headaches, and where each single form of headache is identified via a collection of specific nontrivial diagnostic criteria (see Figure 1). Typically, the diagnostic evaluation of headaches is mainly based on the description of symptoms by the patient. However, the medical history process may be inaccurate and not exhaustive, due to the high number of headache disorders identified by the medical community and characterized via the ICHD-3. Thus, it is of paramount importance in this specific medical field to support clinicians and specialists during the entire diagnostic phase.

As said, a number of approaches in this domain have been already proposed in the literature. The most related ones are briefly discussed next. De Simone et al. (2004) developed AIDA Cefalee, a system consisting of a database for the storage of symptoms and diagnostic data of patients paired with a module that can suggest possible diagnosis but only when all symptoms have been acquired. In particular, the database can be synchronized over the network allowing a continuous sharing of the patients’ information and a cooperation between different research groups. The diagnostic tool has been validated experimentally but no details of the classification method are provided. Simić et al. (2008) presented a novel tool that makes use of rule-based fuzzy logic but is limited to a few forms of disorders. The researchers showed the workflow of the basic rule-based fuzzy logic systems model in which the rules are expressed as a collection of if-then statements. In particular, the information can be extracted by the patients in the form of if-then statements and these rules can be modeled using a fuzzy logic system; once the rules are provided to the system, it can be viewed as an input-to-output mapping. Eslami et al. (2013) proposed a DSS implementing a dynamic questionnaire, but neither the system is publicly available nor the underlying classification method is described. In particular, the system provides questions related to headache disorders and, eventually, derives the most appropriate type of headache using simple human-like algorithmic logic; the accuracy of the diagnosis depends also on the accuracy of the patient’s response. Dong et al. (2014) proposed a general architecture of a DSS based on the ICHD-3 classification. In particular, the researchers’ work is based on a 3-steps translation of the ICHD-3 first in terms of flow-charts, then in terms of an ontological model and, finally, in terms of rules. The system is described mostly from an architectural point-of-view and in-depth details of the translation and of the diagnostic process are not provided. Vandewiele et al. (2018) pro-
1.1 Migraine without aura
Diagnostic criteria:
A. At least five attacks fulfilling criteria B–D
B. Headache attacks lasting 4–72 hours (when untreated or unsuccessfully treated)
C. Headache has at least two of the following four characteristics:
   1. unilateral location
   2. pulsating quality
   3. moderate or severe pain intensity
   4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)
D. During headache at least one of the following:
   1. nausea and/or vomiting
   2. photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.

Fig. 1. Diagnostic criteria of an ICHD-3 diagnosis.

posed a DSS based on machine learning which generates an interpretable predictive model from the collected data. In particular, the system consists of three modules: a mobile application that captures symptomatic data from patients; an automated diagnosis support module that generates an interpretable decision tree, based on data semantically annotated with expert knowledge; and a web application that helps the clinicians to interpret captured data and learned insights by means of visualizations. The diagnostic process is based on supervised machine learning models.

1.2 Motivation and objectives

From the above overview, it should be already clear that none of the existing systems provides, at the same time, (i) the same level of accuracy required by ICHD-3 (ii) a solid, extensible and open knowledge representation model for fully and faithfully representing the ICHD-3 criteria, (iii) a dynamic questionnaire to support clinicians during the entire diagnostic phase, and (iv) an optimization strategy to minimize the number of questions posed to patients. Moreover, (v) none of the aforementioned systems is made available to be tested or used.

To make considerable steps forward in the diagnosis and management of headache disorders, the Italian Ministry of Economic Development appreciated and founded the research project Alcmeone, the main aim of which is providing an innovative organizational and management model, and an advanced technological platform of services for supporting the integrated clinical management of headache patients. In particular, concerning the headache diagnosis, the goal is to develop a decision support system that meets the following five main project specifications: (a) strictly represent ICHD-3 information, structure and criteria; (b) focus on primary headaches, namely, on the first four chapters of the international classification; (c) implement an interactive questionnaire that rigorously guides both clinicians and patients during the medical history process; (d) reach a complete diagnostic picture of each patient by marking each primary headache diagnosis as compatible or not compatible; (e) keep reasonably low the number of questions posed to patients during the medical history process.

1.3 Challenges and contribution

Driven by the lack of effective tools in this domain and by the project specifications, we present in this paper HEAD-ASP, a novel decision support system for the diagnosis of headache disorders. During the development of the system, we faced three main technical challenges: designing a knowledge representation model being able to accommodate domain medical knowledge (of-
testing and using it within research prototype, it is receiving very positive feedback from the group of neurologists that are to a close interaction between clinicians and computer scientists. Indeed, although it is still a made possible thanks to the adoption of a declarative knowledge representation formalism and number of questions that are necessary to complete the diagnostic picture of patients.

Overall, we believe that HEAD-ASP fully meets the real needs in this domain. This has been made possible thanks to the adoption of a declarative knowledge representation formalism and to a close interaction between clinicians and computer scientists. Indeed, although it is still a research prototype, it is receiving very positive feedback from the group of neurologists that are testing and using it within Alcmeone. Some statistics on its effectiveness are reported in Section 5. The system is freely available on-line at https://head-asp.github.io/ichd-dss/.

2 Preliminaries on Answer Set Programming

An ASP atom is of the form \( p(t_1, \ldots, t_k) \), where \( p \) is a predicate symbol and \( t_1, \ldots, t_k \) are terms. A term is either a constant or a variable. Variables start with an uppercase letter, and constants start with a lowercase letter. A literal is an atom \( a_i \) (positive) or its negation \( \neg a_i \) (negative), where \( \neg \) denotes the negation as failure. An ASP program \( \Pi \) is a finite set of rules of the form \( \text{head} \leftarrow \text{body} \), where \( \text{head} \) is a disjunction of atoms \( a_1 \mid \ldots \mid a_n \) with \( n \geq 0 \), and \( \text{body} \) is a conjunction of literals \( b_1, \ldots, b_m \) with \( m \geq 0 \). A rule is called a fact if it has an empty body and a constraint if it has an empty head. An object (atom, rule, etc.) is called ground if it contains no variables. Rules and programs are positive if they contain no negative literals, and general otherwise. Given \( \Pi \), let the Herbrand Universe \( U_\Pi \) be the set of all constants appearing in \( \Pi \) and the Herbrand Base \( B_\Pi \) be the set of all possible ground atoms which can be constructed from the predicate symbols appearing in \( \Pi \) with the constants of \( U_\Pi \). Given a rule \( r, Gr(r) \) denotes the set of rules obtained by applying all possible substitutions \( \sigma \) from the variables in \( r \) to elements of \( U_\Pi \). Similarly, given a program \( \Pi \), the ground instantiation \( Gr(\Pi) \) of \( \Pi \) is the set \( \bigsqcup_{r \in \Pi} Gr(r) \).

For every program, its answer sets are defined using its ground instantiation in two steps: first answer sets of positive programs are defined, then a reduction of general programs to positive ones is given, which is used to define answer sets of general programs. An ASP interpretation \( I \) for \( \Pi \) is a subset of \( B_\Pi \). An interpretation \( M \) is a model for \( \Pi \) if, for every \( r \in Gr(\Pi) \), at least one literal in the head of \( r \) is true w.r.t. \( M \) whenever all literals in the body of \( r \) are true w.r.t. \( M \). A model \( X \) is an answer set (or stable model) for a positive program \( \Pi \) if any other model \( Y \) of \( \Pi \) is such that \( X \subseteq Y \). The reduct or Gelfond-Lifschitz transform of a general ground program \( \Pi \) w.r.t. an interpretation \( X \) is the positive ground program \( \Pi^X \), obtained from \( \Pi \) by (i) deleting all rules \( r \in \Pi \) whose negative body is false w.r.t. \( X \) and (ii) deleting the negative body from the remaining rules. An answer set of \( \Pi \) is a model \( X \) of \( \Pi \) such that \( X \) is an answer set of \( Gr(\Pi)^X \).

Over the years, the ASP language has been extended with additional constructs like strong
negation, weak constraints, function symbols and aggregates (Calimeri et al. 2020). In particular, in this work, we use strong negation and aggregate atoms. A strongly negated atom is an atom that starts with a strongly negation sign (\(-\)), in such case the atom is said to be strongly negated. The semantics of strongly negated atoms is the same of positive atoms (they can appear in heads and can be negated with not in bodies, etc.), with the addition that an answer set can not contain both an atom \(a\) and the strongly negated atom \(-a\).

Aggregates are also useful to model several rules in our context. More in details, an aggregate atom is an expression of the form \(#\text{aggr}(t_1, \ldots, t_m : l_1, \ldots, l_n) \odot u\) where the expression \(#\text{aggr} \in \{\#\text{count}, \#\text{sum}, \#\text{max}, \#\text{min}\}\), \(\odot \in \{<, \leq, =, \neq, >, \geq\}\), \(t_1, \ldots, t_m\) are terms, \(l_1, \ldots, l_n\) are literals and \(u\) is a variable or a number. Intuitively, an aggregate is evaluated by first evaluating the aggregate body \(l_1, \ldots, l_n\), which yields a set of ground tuples of \(t_1, \ldots, t_m\), then the aggregation is computed on the multiset obtained by collecting all the first elements of all tuples and finally the result of the aggregation (according to the specific type of aggregation used) is compared with the term \(u\), yielding the truth value of the aggregate.

3 Knowledge base of the system

In this section we analyze the guidelines in detail identifying the essential aspects for their logic encoding and, then, we propose a representation in ASP.

3.1 ICHD-3: basics

*International Classification of Headache Disorders - 3rd edition* (ICHD-3) provides specific criteria, defined in natural language, for diagnosing known headaches. The possible diagnoses are organized in a hierarchical structure that expresses the existing relations between them. Each type of headache diagnosis includes its own sub-categories, that is, other more specific types of headache, which correspond to a higher level of detail.

The classification consists of 14 chapters grouped into 4 parts. This work focuses on primary headaches (part 1, chapters 1–4) according to the project specifications reported above. Anyway, the designed methodology can be definitely also applied to encode the rest of the diagnoses since they do not differ substantially in the structure. Primary headaches are subdivided into: “Migraine”, “Tension-type headache (TTH)”, “Trigeminal autonomic cephalalgias (TACs)”, and “Other primary headache disorders”. In the following, we describe the structural aspects of the diagnoses, and then we report the main notions that underlie their content.

The diagnosis represents the fundamental structural unit of ICHD-3. Each diagnosis is identified by a set of criteria that appear within a list marked with letters (“A”, “B”, ...). Each criterion includes a series of requirements framed within the symptomatic state of the diagnosis the criterion refers to. A diagnosis is considered compatible if, considering the ailments the patient suffers from, the conditions expressed by all its criteria are met. A criterion can be presented in a monothetic or polythetic form. A criterion is considered monothetic when it identifies a set of specific requirements. The necessary condition for it to be validated is that all its requirements are met. A criterion is considered polythetic when it consists of requirements that appear in an enumerative list format within its own statement. To make such type of criterion as simple as possible, we assign the meaning of sub-criterion to each set of requirements identified by an element of this numbered list (thus, each sub-criterion is marked with a number). The necessary condition for the validation of a polythetic criterion is to verify a minimum number of
sub-criteria on the basis of a fixed inclusion threshold (see Figure 1). A systematic analytical phase was necessary to identify the main notions of the classification. At the basis of ICHD-3 there is the notion of symptom; it can be identified as a key notion because it is involved in the criteria of all the diagnoses of primary headaches. Throughout the systematic analysis of the ICHD-3 contents, we extracted the attributes associated with the symptoms: (i) location of pain (unilateral, bilateral, etc.); (ii) aggravating factors that worsen the pain (such as the movement, etc.) and any limitations caused by pain (such as perform routine physical activities); and (iii) type of pain associated with headache (pulsating, intense, etc.). Furthermore, symptoms can be also characterized by: (i) duration, meant as the persistence over time of the pain caused by a symptom; (ii) frequency of pain attacks, i.e., the number of times the pain caused by a symptom occurs over a specified length of time (such as how many times a day, how many days a month the pain occurs) and, moreover, the (continuous) time interval in which a certain frequency lasts (as an example “headache occurs on 1-14 days/month on average for >3 months”); (iii) number of attacks that affect the patient; and (iv) information relating to the report of a particular clinical exam previously done by the patient.

3.2 ICHD-3: logical representation

In what follows, we encode ICHD-3 diagnoses and criteria via an ASP program $P$ simply using (stratified) negation, aggregates and strong negation. This program builds on a core relational schema consisting of 18 predicates of three different types. Three of these predicates are intensional (type 3) and are used to derive diagnoses, criteria and subcriteria of a specific patient; the remaining ones are extensional. Among the latter, six of them (type 1) are used to represent key notions of ICHD-3 such as all possible diagnoses, symptoms and their attributes; the remaining ones (type 2) are used to encode patients history, such as specific symptoms and the number of their attacks. Hence, all instances of predicates of type 1 and type 3, as well as all rules, are always present in $P$. Conversely, instances of predicates of type 2 vary with patients.

Type 1. As said, this group of predicates models key notions of ICHD-3. We first represent all possible diagnoses, symptoms and attributes via the following binary predicates: ichdDiagnosis(Id, Name), ichdSymptom(Id, Name) and ichdAttribute(Id, Name), where, in all the cases, the first term is an identifier and the second one its name. For example, ichdDiagnosis(d.1.1, “migraine without aura”) represents the diagnosis “1.1. Migraine without aura”, ichdSymptom(s4, “headache”) represents the symptom “headache” identified by code s4, and ichdAttribute(loc2, “bilateral location”) represents the attribute “bilateral location” with its identification code loc2. Moreover, we also make explicit some properties of attributes that are only implicit in ICHD-3. First, there are cases in which the presence of an attribute associated to a specific symptom excludes the possibility to have some other attribute for the same symptom. We use the predicate mutuallyExclusive(Id_attr_1, Id_attr_2) to model such kind of information. For example, if a headache is characterized by a unilateral location, then it cannot be characterized, at the same time, by a bilateral location. Hence, we may have mutuallyExclusive(loc1, loc2) to express the mutual exclusion between the attribute “unilateral location” identified by code loc1 and the attribute “bilateral location” identified by code loc2. Clearly, these two identifiers occur in two facts of the form: ichdAttribute(loc1, “unilateral location”) and ichdAttribute(loc2, “bilateral location”). Similarly, we also have sameAs(Id_attr_1, Id_attr_2) to specify that, if an attribute is associated with a specific symptom, then, at the same time, also the attribute semantically equiv-
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ICHD-3 often uses different synonymous terms in different diagnostic criteria; without modeling such similarities our encoding would not completely reflect the intended ICHD-3 meaning. For example, we include in $\mathcal{P}$ sameAs(int2, int10), ichdAttribute(int2, “strong intensity”), and ichdAttribute(int10, “acute intensity”). Finally, we represent the dependence between diagnoses, symptoms and attributes via the predicate isA(Id1, Id2). An example concerning the symptoms is the atom isA(s18, s54), where s18 and s54 are provided by ichdSymptom(s18, “diplopia”) and ichdSymptom(s54, “visual symptom”).

Type 2. In this group we have predicates used to encode patients history. We start with symptom(Id_sym) and symAttribute(Id_sym, Id_attr), modelling the fact that a patient has a specific symptom and the fact that his/her symptoms have some peculiarity modeled via what we called attributes (e.g., symptom location, pain type); for example, symptom(s4) and symAttribute(s4, loc2) represent that the patient reported the symptom “headache” with the attribute “bilateral location”; indeed, ichdSymptom(s4, “headache”) and ichdAttribute(loc2, “bilateral location”) hold. We also use the predicates minAttacks(Id_sym, Value) and maxAttacks(Id_sym, Value) to specify that the actual number of attacks of a patient’s symptom falls in a certain range; for example minAttacks(s4, 5) (resp. maxAttacks(s4, 10)) indicates that the patient reported at least “5” (resp. at most “10”) attacks associated with the symptom identified by code s4. Similarly, we use the predicates minDuration(Id_sym, Value) and maxDuration(Id_sym, Value) to specify the duration of the pain caused by a certain symptom. As an example, minDuration(s4, 240) (resp. maxDuration(s4, 4320)) specify that the patient reported that the symptom s4 lasts at least 240 (resp. at most 4320) minutes. In the same way, frequency of pain attacks that are associated to a certain symptom is modeled by means of the predicates minDaysPerMonth(Id_sym, Value) and maxDaysPerMonth(Id_sym, Value). Finally, we use the predicate reportedCriterion(Description) to model some portions of text for which it was not possible and convenient to identify a decomposed modeling. Indeed, they express peculiar assertions only of certain diagnoses, occurring infrequently within the domain or, when reported, do not present syntactic or semantic variations. The only term of this predicate is the textual description of the statement. For example, reportedCriterion (“At least one first or second degree family member has had attacks that meet the criteria of hemiplegic migraine”) expresses the presence of the specified statement.

Type 3. Predicates in this group have the following signature: diagnosis(Id), criterion(Id_diag, Letter), subCriterion(Id_diag, Letter_crit, Number). They model the identifiers of diagnoses, criteria and subcriteria that can be derived for a specific patient. As an example, if the atom diagnosis(d.1.1) can be derived from $\mathcal{P}$, this means that the ICHD-3 diagnosis “1.1. Migraine without aura” is compatible with patient history. Likewise, the derivation of the atom criterion(d.1.1, “A”) means that criterion “A” of “1.1. Migraine without aura” is compatible with patient history, namely, the patient reported “at least five attacks fulfilling criteria B-D”. Finally, the derivation of the atom subCriterion(d.1.1, “C”, 1) means that subcriterion “1” of criterion “C” of “1.1. Migraine without aura” is compatible with patient history, namely, the patient reported that headache has the characteristic “unilateral location”.

Rules. As shown in the previous subsection, the diagnoses are organized in a hierarchical structure which expresses the specialization-generalization relations existing between them (Figure 2). Intuitively, if a more specific diagnosis is compatible, then it is possible to infer a more generic
diagnosis (the former being a sub-type of the latter); conversely, if a higher level diagnosis is not compatible, all its related specializations are invalidated. The following rules, among the others, express the implications inferable from the relations between diagnoses.

\[ r_1 : \text{diagnosis}(Id_{sup}) \leftarrow \text{diagnosis}(Id), \text{isA}(Id, Id_{sup}). \]
\[ r_2 : \neg \text{diagnosis}(Id) \leftarrow \neg \text{diagnosis}(Id_{sup}), \text{isA}(Id, Id_{sup}). \]

The two rules shown below define the conditions that must be met so that the diagnosis “1.1. Migraine without aura” can be compatible or not compatible (Figure 1). Intuitively, rule \( r_3 \) derives the diagnosis as true (compatible) if all its criteria “(A-D)” are true. Similarly, rule \( r_4 \) expresses that the diagnosis is certainly false (not compatible) if at least one of its criteria is certainly false. Note that to use the strong negation is quite convenient to model such scenarios in which we need to distinguish criteria and diagnoses that are definitely confirmed from those definitely disconfirmed and from those still undefined, without any need in adding new predicates and further constants. This is also reflected to the predicates encoding patient’s symptomatology.

\[ r_3 : \text{diagnosis}(Id) \leftarrow \text{ichdDiagnosis}(Id, “migraine without aura”), \text{criterion}(Id, “A”), \text{criterion}(Id, “B”), \text{criterion}(Id, “C”), \text{criterion}(Id, “D”). \]
\[ r_4 : \neg \text{diagnosis}(Id) \leftarrow \neg \text{ichdDiagnosis}(Id, “migraine without aura”), \neg \text{criterion}(Id, “.”). \]

Each criterion (resp. subcriterion) of ICHD-3 is encoded through rules whose head is constituted by the predicate criterion (resp. subcriterion), while the body models effectively the semantics of the statement of the criterion (resp. sub-criterion), on the basis of its informal description in the international classification. As an example, consider criterion “B” of diagnosis “1.1”: “Headache attacks lasting 4-72 hr”. The following rules model such monothetic criterion. Declaratively, rule \( r_5 \) states that if the symptom “headache” is true and its duration respects the specified time interval, then criterion(d.1.1, “B”) will be derived as true. Rules \( r_6, r_7, r_8 \) express the conditions according to which the criterion is certainly false.

\[ r_5 : \text{criterion}(Id, “B”) \leftarrow \text{ichdDiagnosis}(Id, “migraine without aura”), \text{ichdSymptom}(Id_{sym}, “headache”), \text{symptom}(Id_{sym}), \text{minDuration}(Id_{sym}, 240), \text{maxDuration}(Id_{sym}, 4320). \]
\[ r_6 : \neg \text{criterion}(Id, “B”) \leftarrow \text{ichdDiagnosis}(Id, “migraine without aura”), \neg \text{ichdSymptom}(Id_{sym}, “headache”), \neg \text{symptom}(Id_{sym}), \neg \text{minDuration}(Id_{sym}, 240). \]
Consider criterion “C” of diagnosis “1.1”: “Headache has at least two of the following four characteristics: (i) unilateral location; (ii) pulsating quality; (iii) moderate or severe pain intensity; (iv) aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)” The following portion of the program corresponds to the encoding of such polythetic criterion.

\[
\begin{aligned}
\text{r}_7 : & \text{criterion}(Id, \text{"B"}) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \text{ichdSymptom}(Id, \text{sym}, \text{"headache"}), \text{symptom}(Id, \text{sym}), \text{maxDuration}(Id, \text{sym}, 4320).
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_8 : & \text{criterion}(Id, \text{"B"}) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \text{ichdSymptom}(Id, \text{sym}, \text{"headache"}), \neg \text{symptom}(Id, \text{sym}).
\end{aligned}
\]

In this case, for a more natural modeling, it was convenient to use the aggregation construct \#count. In particular, the rule \text{r}_9 aggregates the satisfied subcriteria and counts them (\#count) in order to check if the resulting value matches the number required by the criterion itself. It can be noted that the rules that express the conditions according to which the predicate in the head is certainly false can be automatically generated by denying, one at a time, the predicates of type 2.

\[
\begin{aligned}
\text{r}_9 : & \text{criterion}(Id, \text{"C"}) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \#\text{count}\{X : \text{subCriterion}(Id, \text{"C"}, X)\} \geq 2.
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_{10} : & \text{criterion}(Id, \text{"C"}) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \#\text{count}\{X : \neg \text{subCriterion}(Id, \text{"C"}, X)\} \geq 3.
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_{11} : & \text{subCriterion}(Id, \text{"C"}, 1) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \text{ichdSymptom}(Id, \text{sym}, \text{"headache"}), \text{symptom}(Id, \text{sym}), \\
& \text{symAttribute}(Id, \text{sym}, \text{Id_attr}), \text{ichdAttribute}(\text{Id_attr}, \text{"unilateral location"}).
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_{12} : & \neg \text{subCriterion}(Id, \text{"C"}, 1) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \text{ichdSymptom}(Id, \text{sym}, \text{"headache"}), \neg \text{symptom}(Id, \text{sym}).
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_{13} : & \neg \text{subCriterion}(Id, \text{"C"}, 1) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \text{ichdSymptom}(Id, \text{sym}, \text{"headache"}), \text{symptom}(Id, \text{sym}), \\
& \neg \text{symAttribute}(Id, \text{sym}, \text{Id_attr}), \text{ichdAttribute}(\text{Id_attr}, \text{"unilateral location"}).
\end{aligned}
\]

In this case, for a more natural modeling, it was convenient to use the aggregation construct \#count. In particular, the rule \text{r}_9 aggregates the satisfied subcriteria and counts them (\#count) in order to check if the resulting value matches the number required by the criterion itself. It can be noted that the rules that express the conditions according to which the predicate in the head is certainly false can be automatically generated by denying, one at a time, the predicates of type 2.

\[
\begin{aligned}
\text{r}_9 : & \text{criterion}(Id, \text{"C"}) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \#\text{count}\{X : \text{subCriterion}(Id, \text{"C"}, X)\} \geq 2.
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_{10} : & \text{criterion}(Id, \text{"C"}) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \#\text{count}\{X : \neg \text{subCriterion}(Id, \text{"C"}, X)\} \geq 3.
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_{11} : & \text{subCriterion}(Id, \text{"C"}, 1) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \text{ichdSymptom}(Id, \text{sym}, \text{"headache"}), \text{symptom}(Id, \text{sym}), \\
& \text{symAttribute}(Id, \text{sym}, \text{Id_attr}), \text{ichdAttribute}(\text{Id_attr}, \text{"unilateral location"}).
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_{12} : & \neg \text{subCriterion}(Id, \text{"C"}, 1) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \text{ichdSymptom}(Id, \text{sym}, \text{"headache"}), \neg \text{symptom}(Id, \text{sym}).
\end{aligned}
\]

\[
\begin{aligned}
\text{r}_{13} : & \neg \text{subCriterion}(Id, \text{"C"}, 1) \leftarrow \text{ichdDiagnosis}(Id, \text{"migraine without aura"}), \\
& \text{ichdSymptom}(Id, \text{sym}, \text{"headache"}), \text{symptom}(Id, \text{sym}), \\
& \neg \text{symAttribute}(Id, \text{sym}, \text{Id_attr}), \text{ichdAttribute}(\text{Id_attr}, \text{"unilateral location"}).
\end{aligned}
\]

4 The next question strategy

As said in the Introduction, the goal is to develop a decision support system implementing a questionnaire that: (i) rigorously guides both clinicians and patients during the medical history process; (ii) automatically adapts to patients; and (iii) reaches, in a reasonable amount of time, a complete diagnostic picture by inferring every diagnosis as either compatible or not compatible. To this end, to satisfy (i), we formulate each possible question as binary (i.e., their answers are simply “yes” or “no”) to overcome the typical fact that patients are not always able to adequately describe their disorders. Moreover, we design a logical module —on top of the [ICH-D-3] encoding of Section 3.2— that, at each step of the questionnaire, identifies the convenient next question described in the following. To satisfy (ii), we discard from the set of candidate next questions those that are inappropriate or irrelevant (an example of an inappropriate question is a question related to the presence of the symptom “diplopia” if the patient already reported not to have the symptom “visual disorder”; an example of an irrelevant question is a question concerning a diagnosis that has already been inferred as not compatible.) To satisfy (iii), we implement a greedy strategy that first computes, for each candidate next question, the minimum number of inferred diagnoses when considering both the “yes” or “no” answer and then, among these values, it selects the maximum one along with its associated question.
Algorithm 1: Questionnaire process

**Input:** An ASP encoding $\Pi = \Pi_{ichd} \cup \Pi_q$, where $\Pi_{ichd}$ is the encoding that models the ICHD guidelines and $\Pi_q$ is the encoding that implements the questionnaire logic

**Output:** A set of compatible diagnosis $C$, a set of not compatible diagnosis $N$, s.t. $C \cup N$ is the set of all diagnosis encoded in $\Pi_{ichd}$

```
begin
  U = possibleDiagnosis($\Pi_{ichd}$)
  H = \emptyset, C = N = \emptyset
  while C \cup N \neq U do
    $\Pi' = \Pi_{ichd} \cup H$
    $S = \text{solveUnique}(\Pi')$
    $C = \{c \in S \mid \text{predicate}(c) = \text{diagnosis} \land \text{isPositive}(c)\}$
    $N = \{c \in S \mid \text{predicate}(c) = \text{diagnosis} \land \text{isNegative}(c)\}$
    if $C \cup N \neq U$ then
      $\Pi'' = \Pi_{ichd} \cup \Pi_q \cup H$
      $\mathcal{F} = \text{solve}(\Pi'')$
      $Q = \bigcup_{c \in \mathcal{F}} \{c \in S \mid \text{predicate}(c) = \text{ask}\}$
      $B_{\text{score}} = -1, B_q = \perp$
      forall $q \in Q$ do
        $d_{\text{yes}} = \text{getDeterminedDiagnosisCount}(q, \text{yes}, \mathcal{F})$
        $d_{\text{no}} = \text{getDeterminedDiagnosisCount}(q, \text{no}, \mathcal{F})$
        $q_{\text{score}} = \min(d_{\text{yes}}, d_{\text{no}})$
        if $q_{\text{score}} > B_{\text{score}}$ then
          $B_{\text{score}} = q_{\text{score}}, B_q = q$
      $H = H \cup \text{patientAnswer}(B_q)$
  return C, N
```

Architecture of the questionnaire. Algorithm 1 presents the questionnaire process as implemented in our system. The algorithm takes as input the ASP encoding of $\Pi_{ichd}$, as described in the previous section, and the ASP encoding that implements the questionnaire logic ($\Pi_q$) as described in the next paragraphs. The output is composed of the set of compatible diagnoses $C$ and the set of not compatible diagnoses $N$ according to the history of answers $H$ provided by the patient, where $H$ is a set of ASP facts. Note that, the history of answers is collected during the process. Initially, at line 2 the algorithm retrieves the set of all possible diagnoses encoded in $\Pi_{ichd}$ and then initializes the patient’s history of answers, the set of compatible answers, and the set of not compatible answers to the empty set (line 3). Then, the algorithm loops until all diagnoses are determined (line 4). At each iteration, first the algorithm computes the current diagnostic status, i.e., the current set of compatible diagnoses and the current set of not compatible diagnoses, by running the $\Pi_{ichd}$ encoding together with the history of answers provided by the patient. To denote the fact that $\Pi_{ichd} \cup H$ has a unique answer set, we denote the solving method with solveUnique (line 6). At this point, the algorithm checks whether there are still diagnoses that are not determined: in the negative case it finishes, and in the positive case it computes the next question to be posed to the patient (from line 9 to 20). To do so, it first builds an ASP program $\Pi''$ as the union of $\Pi_{ichd}, \Pi_q$ and $H$. At line 10, it stores the answer sets of $\Pi''$ into a variable $\mathcal{F}$. There are $2n$ answer sets, where $n$ is the number of questions selected at the current step (further details later in this section): given a selected question $q$, there is exactly one answer set where $q$ is asked and the answer to $q$ is affirmative, and exactly one answer set where $q$ is asked and the
answer to \(q\) is negative. The set of selected questions is \(Q\), which is computed by putting together the atoms (exactly one instance per \(\text{answer set}\)) whose predicate is \(\text{ask}\) (line 12). From line 13 to 19, the algorithm computes, heuristically, the best question (\(B_q\) in the algorithm) to pose to the patient, according to the worst-case minimization strategy discussed above. Initially, the best question \(B_q\) is initialized to \(\perp\) to denote the fact that it has no initial value, and the score is initialized to \(-1\) (line 13). For each question \(q\), the algorithm finds the number \(d_{\text{yes}}\) of determined diagnoses of \(q\) if answered affirmatively (line 15) and the number \(d_{\text{no}}\) of determined diagnoses of \(q\) if answered negatively (line 16). The function \(\text{getDeterminedDiagnosesCount}(q, \text{answer}, \mathcal{S})\) essentially finds the \(\text{answer set}\) in \(\mathcal{S}\) where \(q\) is asked and the answer to \(q\) is \(\text{answer}\) and returns the number of determined diagnoses in that \(\text{answer set}\). The score of \(q\) is the minimum between \(d_{\text{yes}}\) and \(d_{\text{no}}\). In other words, a question is scored by the number of diagnoses that are determined in the worst-case scenario. The selected question \(B_q\) is the question having the maximum score (lines 18 to 19). Finally, the selected best question \(B_q\) is posed to the patient and their answer is added to the history \(H\) (line 20): the function \(\text{patientAnswer}(B_q)\) asks \(B_q\) to the patient and returns their answer encoded as an ASP fact.

**ASP encoding.** In the following, we enumerate and give an informal semantics of the predicates defined in the ASP program that implements the questionnaire described above. Based on the notions that appear in the diagnostic criteria classified in the previous section and that will be the subject of the questions to be asked, we identified a set of topics that allow us to split the set of potential questions into groups. In the encoding that implements the questionnaire, we listed such topics in the form of instances of the predicate \(\text{topic}(T, D)\), where, the variable \(T\) is instantiated by the constants that identify the topics, and \(D\) is either instantiated by the constant \(\text{dependent}\) or \(\text{independent}\) to indicate that a topic is related to a symptom or not. An example of a ground instance of the predicate \(\text{topic}\) is \(\text{topic}\)(\(\text{duration}, \text{dependent}\)), which represents that \(\text{duration}\) is a dependent notion (e.g., the duration of headache or nausea makes sense, while duration alone does not). On the other hand, a symptom is a notion that is not dependent on another concept and we express it by the ground instance \(\text{topic}(\text{symptom}, \text{independent})\). The instances of the predicate \(\text{criterionDependsOn}(\text{Id}_{\text{diag}}, \text{Letter}, X, Y, \text{Topic})\) express the dependence of a diagnostic criterion \(\text{Letter}\) of a diagnosis \(\text{Id}_{\text{diag}}\), on the elements \(X\) and \(Y\) that characterize the topic \(\text{Topic}\) and that will constitute the possible subject of a question. For example, we use \(\text{criterionDependsOn}(\text{d.2.1}, \text{D}, \text{s33}, \text{nausea}, \text{symptom})\) to denote that the criterion \(\text{D}\) of the diagnosis \(\text{d.2.1}\) depends on the symptom \(\text{nausea}\), whose identifier is \(\text{s33}\). Each possible subject of the question is collected in the ground instances of the predicate \(\text{possible}\) through the following rule:

\[
\text{r14} : \text{possible}(X, Y, \text{Topic}) \leftarrow \text{criterionDependsOn}(\text{Id}_{\text{diag}}, \text{Letter}, X, Y, \text{Topic}).
\]

The predicate \(\text{possible}\) is then used to generate the predicate \(\text{ask}(X, Y, \text{Topic})\) in the portion of the disjunctive program in which we evaluate asking potential questions. To the independent type topics correspond instances of the predicate \(\text{possible}\) in which \(X\) and \(Y\) are the characterizing elements, identified and formalized in the previous section. As an illustration, the characterizing elements of the topic \(\text{exam}\) are its name and the relative report, so, an example of its instantiation is \(\text{possible}(\text{gene CACNA1A}, \text{presence of mutation}, \text{exam})\). In the case of independent type topic, it is necessary to represent the name of the symptom the topic refers to. Therefore, the variable \(X\) is instantiated by the name of the symptoms and the variable \(Y\) by the elements that characterize the topic itself. An example for the topic \(\text{duration}\) is the atom \(\text{possible}(\text{headache}, 5, \text{duration})\) where, “5” is one of the values, belonging to the considered domain, expressed in
minutes. We define “relevant” an element present in a criterion relating to at least one diagnosis not yet excluded and relating to a diagnosis “child” (according to predicate isA) whose diagnosis “father” has been confirmed.

\[ r_{15} : \text{relevant}(X, Y, \text{Topic}) \leftarrow \text{criterionDependsOn}(\text{Id}_\text{diag}, \text{Letter}, X, Y, \text{Topic}), \not\text{criterion}(\text{Id}_\text{diag}, \text{Letter}), \not\text{diagnosis}(\text{Id}_\text{diag}), \text{isA}(\text{Id}_\text{diag}, \text{Id}_\text{sup}_\text{diag}), \text{diagnosis}(\text{Id}_\text{sup}_\text{diag}). \]

The patient’s answers will be collected in the ground instances of the predicate answer(X, Y, Topic, Answer, Type) where Answer is either the constant true or false and the variable Type is instantiated by the constant real or simulated to distinguish between the history of answers actually given by the patient and the answers simulated during the evaluation phase for the choice of the next question. The logic module that implements the interactive questionnaire is structured by following the “Guess and Check” programming paradigm of ASP. The “Guess” part of the questionnaire program is composed of a set of disjunctive rules that allow to consider the different possibilities for the choice of the next question. On the other hand, the “Check” part consists of a set of constraints that discard the unwanted models (e.g., models which ask more than one question simultaneously, models in which the question has already been asked or models in which the question is no more relevant). Beside disjunctive rules and constraints, ASP programs are also composed of a set of normal rules (i.e., rules with a single atom in the head) that are used to propagate knowledge in the program (e.g., propagate the consequences of an answer). The program identifies a set of \( n \) questions that could be asked and, in order to analyze separately the consequences of the 2 possible answers from the patient, it generates \( 2n \) answer sets. In other words, for each of the \( n \) possible questions, the program outputs an answer set that represents the outcome of the affirmative answer and an answer set that represents the outcome of the negative answer. Overall, an answer set represents a possible world in which the system can evolve once the patient answers another question. The following disjunctive rules compose the “Guess” part. In particular, for each topic \( T \) considered, we choose it or we don’t choose it \( (r_{16}) \), for an independent type topic \( T \), we ask, or we don’t, a possible question regarding \( T \) \( (r_{17}) \), given a dependent type topic \( T \) and a possible question regarding it, after verifying the presence of the symptom the topic refers to, we ask the question or we don’t \( (r_{18}) \), we simulate the patient’s answer to each question when it is affirmative and when it is negative \( (r_{19}) \), and we exclude the evaluation, in the same set, of more than one question \( (r_{20}) \):

\[ r_{16} : \text{chosenTopic}(T) \leftarrow \text{chosenTopic}(T) \leftarrow \text{topic}(T,D). \]
\[ r_{17} : \text{ask}(X,Y,T) \leftarrow \text{chosenTopic}(T), \text{possible}(X,Y,T), \text{topic}(T, \text{independent}). \]
\[ r_{18} : \text{ask}(\text{Name},Y,T) \leftarrow \text{chosenTopic}(T), \text{possible}(\text{Name},Y,T), \text{topic}(T, \text{dependent}), \text{ichdSymptom}(\text{Id}, \text{Name}), \text{symptom}(\text{Id}). \]
\[ r_{19} : \text{answer}(X,Y,T, \text{false}, \text{simulated}) \text{answer}(X,Y,T, \text{true}, \text{simulated}) \leftarrow \text{ask}(X,Y,T). \]
\[ r_{20} : \not \#\text{count}\{X,Y,T : \text{ask}(X,Y,T)\} = 1. \]

In the following, we present the main constraints that allow a resizing of the admissible questions set, in order to let them conform to the history of answers. In particular, not relevant questions cannot be asked \( (r_{21}) \), a question that has been previously answered cannot be asked \( (r_{22}) \), and it is not possible to consider, in a question, a numerical value for the duration of a symptom that is
not in the previously identified range \((r_{23})\):

\[
\begin{align*}
    r_{21} & : \leftarrow \text{ask}(X,Y,T), \ not \ relevant(X,Y,T). \\
    r_{22} & : \leftarrow \text{ask}(X,Y,T), \ \text{answer}(X,Y,T; \text{real}). \\
    r_{23} & : \leftarrow \text{ask}(\text{Name},V,\text{duration}), \ \text{ichdSymptom}(Id,\text{Name}), \ \text{symptom}(Id), \\
                 \ \text{minDuration}(Id,Y), \ V < Y.
\end{align*}
\]

The program contains also other rules similar to \(r_{23}\) focusing on different numerical parameters. By simulating the patient’s answer, we evaluate the effect that such answer would have in the process of determining the diagnoses. We use the information that would be acquired through the answers to activate the corresponding predicates which, once propagated in the ICHD-3 encoding, contribute to inferring the eventual compatible and not compatible diagnoses. The patient’s affirmative answer concerning a symptom activates the predicate which models its presence.

\[
r_{24} : \text{symptom}(Id) \leftarrow \text{answer}(Id,\text{symptom, true, }).
\]

On the other hand, the patient’s negative answer concerning a symptom allows us to infer the absence (modeled with strong negation) of the predicate which models its presence.

\[
r_{25} : \neg \text{symptom}(Id) \leftarrow \text{answer}(Id,\text{symptom, false, }).
\]

Finally, we compute the number of diagnoses that would be determined. To do so, we use the aggregation construct \#count: we count the diagnoses that would be compatible and those ones that would be not compatible.

\[
\begin{align*}
    r_{26} & : \text{compatibleDiag}(N) \leftarrow \#\text{count}\{Id : \text{diagnosis}(Id)\} = N. \\
    r_{27} & : \text{notCompatibleDiag}(N) \leftarrow \#\text{count}\{Id : \neg \text{diagnosis}(Id)\} = N.
\end{align*}
\]

The number of determined diagnoses is then inferred by the following rule:

\[
r_{28} : \text{determinedDiag}(D) \leftarrow \text{compatibleDiag}(N), \ \text{notCompatibleDiag}(M), \ D = N + M.
\]

Such a value is then used by Algorithm 1 as previously discussed.

### 5 System implementation and testing

The decision support system has been implemented into two Web applications: a REST Web service, and a Web graphical interface. Web applications are one of the most common types of distributed applications. In general, they are accessible without requiring any installation process and are cross-platform by design.

Figure 3 presents, with an example, the architecture of Head-ASP. The user (a physician) interacts with the Web Graphical Interface which communicates under the form of HTTP requests and responses with the Web Service. The HEAD-ASP Web Service exposes to the Web the functionalities of the DSS. It provides an HTTP method that receives a user answers history and returns the current diagnosis and the next question, implementing the algorithm presented in the previous section in Algorithm 1. The Web Service is not intended to be used directly by humans, but it is instead intended to be invoked by other programs. It has been implemented in JAVA using Spring, which is a well-known framework for Web development. We used DLV (Alviano et al. 2017) as the ASP solver of the application.

The implemented service follows the REST architectural style (Richardson and Ruby 2008).
concept of state or session, and thus it can scale well horizontally (Michael et al. 2007): more instances can be deployed simultaneously and which instance is handling a request is not important. The Web service also exposes a documentation that shows its communication protocol, i.e., how to invoke it and how to interpret its output. In simple terms, the Web service exposes a method that accepts a patient history of answers and returns the current diagnosis and the next question. The response contains special tokens in the cases where the questionnaire is completed (i.e., every diagnosis is either compatible or not compatible) or the questionnaire cannot be continued (i.e., there is no relevant question to ask).

The HEAD-ASP Web graphical interface demonstrates the functionalities of the DSS and, contrary to the Web service, it is intended to be used by humans. Currently, it is used as the primary interface of HEAD-ASP until the future integration of the DSS in the Alcmeone project platform. To develop the Web interface we used Angular 8, which is a popular JavaScript framework for the development of Web graphical interfaces. The Web interface and the Web service (and its documentation) are available at [https://head-asp.github.io/ichd-dss](https://head-asp.github.io/ichd-dss).

To minimize the number of defects in the implementation and investigate the performance of the approach, we implemented a testing framework where questions are answered randomly. In this section, we report the results obtained by the current release of HEAD-ASP on approximately 7400 questionnaires. Among these, we focused on those –3000 in total– that led to at least one headache disorder, which are representative of real cases of headache. Figure 4 shows two histograms summarizing the results of our tests. In both histograms, each bar on top of a value represents how many questionnaires had a length x. In (a), we plot the distribution of the number of questionnaires by overall length (i.e., the length necessary to reach a complete diagnostic picture); in (b), we consider the distribution of the number of questionnaires by the length at which the first compatible diagnosis has been reached. The average length is of 21.44 questions in the...
first case and of 12.99 in the second one. It is worth noting that these results are in line with the neurologists’ experience and expectations. Finally, considering the fact that there are more than 150 candidate questions encoded in the system, the results of our experiment reveal how HEAD-ASP is able to effectively discard unnecessary questions when needed, pruning the search space and producing short questionnaires.

6 Discussion and future work

In this paper, we have presented HEAD-ASP: a novel decision support system for the diagnosis of headache disorders —one of the most common and disabling conditions of the nervous system throughout the world. The system is currently tested by a group of neurologists that are profitably using it within Alcmeone —a research project whose objective is providing an innovative organizational and management model, and an advanced technological platform of services for supporting the integrated clinical management of headache patients.

Although design and implementation of the DSS was quite challenging, we found very natural to use logic programming both to encode the ICHD classification and to model the heuristics for determining the next question. In particular, the advantages can be summarized as follows: (i) simple and complex diagnoses can be encoded in a natural and precise way; (ii) ICHD updates can be easily and locally transferred to the encoding; (iii) medical knowledge can be represented and integrated in a declarative way; and (iv) identifying candidate questions and simulating their effects are tasks that can be carried out in the same framework. Moreover, concerning the adoption of ASP w.r.t. other languages such as Prolog, we feel that a bottom-up paradigm here is more appropriate since we start from some domain knowledge, we add patient’s symptoms, we derive compatible and not compatible criteria, and we identify compatible and not compatible diagnoses. Moreover, we do not have a specific query to evaluate but each time we have to update our diagnostic picture marking each diagnosis as compatible, not compatible or not-yet-determined.

Concerning our future plans, the ultimate objective is to promote the system inside the Italian Society for the Study of Headache (SISC) so that it can become a valid support to clinicians and specialists. To this end, we are still refining and improving it according to the feedback we are currently receiving. In particular, the next steps include: (i) completing the ICHD-3 encoding; (ii) analyzing the next-question problem from a theoretical perspective; (iii) further reducing the average number of questions needed to reach a complete diagnosis. Least but not last, we would like to generalize our methodology to be easily applicable in similar contexts.
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