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## Agent-Based Reasoning in Medical Planning and Diagnosis Combining Multiple Strategies

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Medical reasoning describes a form of qualitative inquiry that examines the cognitive (thought) processes involved in making medical decision. In this field the goal for diagnostic reasoning is assessing causes of observed conditions in order to make informed choices about treatment. In order to design a diagnostic reasoning method we merge ideas from a hypothetic-deductive method and the Domino model. In this setting, we introduce the so called Hypothetic-Deductive-Domino (HD-D) algorithm. In addition, a multi-agent approach is presented, which takes advantage of the HD-D algorithm for illuminating different standpoints in a diagnostic reasoning and assessment process, and for reaching a well-founded conclusion. This multi-agent approach is based on the so called Observer and Validating agents. The Observer agents are supported by a deductive inference process and the Validating agents are supported by an abductive inference process. The knowledge bases of these agents are captured by a class of possibilistic logic programs. Hence, these agents are able to deal with qualitative information. The approach is illustrated by a real scenario from diagnosing dementia diseases.

*Keywords:* Medical Diagnosis; Decision Making; Knowledge Representation and Reasoning.

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## 1. Introduction

In medicine the goal for diagnostic reasoning is assessing causes of observed conditions in order to make informed choices about treatment. The knowledge about causes of diseases is preferably created in randomized clinical trials, generating *Evidence-Based Medical* (EBM) knowledge. This knowledge is based on probabilities, *e.g.*, if there is evidence that a certain disease is causing a given observed or measured phenomenon in a proportion of all cases of this disease. In addition, knowledge about the proportion of the manifested phenomenon in the total population is needed, including subjects not having the disease in order to assess the diagnostic value of the observation. If the observation has a high diagnostic value (*i.e.*, seen in a large proportion of cases with the disease and in a low proportion of cases without the disease) it is typically included in *Clinical Guidelines* (CGs) for diagnosis. A CG is a structured document, containing detailed advice on the management of a particular disorder or group of disorders, aimed at health-care professionals.

In practice, the clinical guidelines are interpretations of the EBM knowledge, aiming to overcome ambiguities and incompleteness of the available and evolving domain knowledge. One can view the evidence-based, statistically based, medical knowledge as being the generic knowledge about a medical domain, but it is often of a limited aid in assessing an individual's condition.

Due to the ambiguities in and incompleteness of a medical knowledge domain, the clinical guidelines often apply expressions that mirror the status of the knowledge (*e.g.*, *possible*, *probable*, *supporting*, *unlikely*, *etc.*). Even in the case when a CG uses apparently firm statements of presence or absence, it is commonly known in this case as *tacit* knowledge that some assessments cannot be necessarily true. For instance, the major clinical guideline for assessing mental conditions<sup>1</sup> states that Alzheimer's disease is present or not based on a set of observations, but only if all other medical conditions potentially causing the observed cognitive deficits are excluded. From an epistemic perspective, and in practice, it is impossible to undoubtedly exclude all other potential causes, meaning that Alzheimer's disease will never be assessed, and the clinical guideline would be useless. Nevertheless, Alzheimer's disease is known to cause about 70% of all cases of dementia, which allows also a highly unskilled physician to assess some dementia cases correctly, even if s/he does not know about any other condition causing dementia. On the other hand, considering that Alzheimer's disease is a fatal condition, typically leading to death within 5-8 years after receiving the diagnosis, the individuals who actually have dementias that can be *cured*, should not have to suffer from a misdiagnosed Alzheimer's disease. In fact, studies using autopsy as gold standard for dementia diagnosis have shown that only 49 % receives a correct diagnosis when first diagnosed by experts, and in 37 % of the cases the diagnosis was changed completely<sup>4</sup>.

Diagnosis is not as much about what a clinician *knows* about a domain, but *knowing what to do*, and knowing *how to apply* the available knowledge<sup>37</sup>. Diag-

nosis is primarily a problem-solving process. The skills to perform it differ among clinicians depending on education, training, experience (*i.e.*, level of expertise) and contextual factors such as workload and work content. It is shown that novice doctors tend to reason using a causal procedure (starting with a potential diagnosis and searching for evidence to prove this condition), following the EBM knowledge they have acquired during medical education. In addition, it has been shown that experienced physicians tend to use a causal reasoning when explaining assessments to *e.g.*, medical students<sup>37</sup>. However, the risk to miss important information is high when relying only on causal knowledge when conducting assessment. The diagnostic reasoning process applied by experts is described as a process where observations are typically collected without jumping to conclusions too early, in a process of creating the base for moving forward towards a diagnosis. Typically, at the point when hypotheses are formulated, the hypotheses finally selected are included with the set of experts' reasoning, which is not necessarily the case with novice doctors' reasoning<sup>37</sup>.

Consequently, a much desired property of a medical diagnostic support system is to be able to support the diversity of human reasoning in the diagnostic problem-solving process and potentially aid the transformation from novices' type of reasoning towards applying diagnostic reasoning rather than causal reasoning. Hence, by combining two kinds of reasoning (*deductive and abductive reasoning*), one can resemble when needed the reasoning type of novice and expert doctors. Other essential properties are the capability to handle comorbidity manifested in patients, and be able to capture the incomplete, ambiguous and uncertain medical knowledge. Comorbidity may imply the expertise in several very diverse medical specialities. The modeling of all these *knowledges* needs to be done by medical professionals, this requires formalisms that are intuitive and transparent to capture the model. To achieve this, rich methods for capturing medical knowledge are required.

The identification of general methods which could support the diagnostic process is a crucial challenge for the new generation of medical support systems. In the design of tools for medical diagnosis reasoning at least one can identify three important challenges:

- (1) How to capture and combine medical knowledge from different types of medical sources such as clinical guidelines and evidence-based medical literature?
- (2) How to manage the medical knowledge in order to increase the quality of a medical diagnosis?
- (3) How to make the diagnostic process support transparent to medical professionals with different level of expertise, and by this providing an opportunity to develop their expertise?

As we have argued, clinical guidelines usually are pervaded of qualitative information. In the literature, one can find different approaches for encoding qualitative information<sup>26,38,40</sup>. A common strategy for capturing qualitative information is by using non-numerical values. Possibilistic reasoning has shown to be a suitable ap-

proach for dealing with qualitative reasoning<sup>38</sup>. In particular, the possibilistic values of a possibilistic knowledge can be non-numerical values which can capture the uncertainty of a knowledge base. In the context of logic programming, there is an extension of answer set programming (ASP)<sup>3</sup> which combine possibilistic logic with a non-monotonic inference<sup>34</sup>. This extension of ASP is able to capture non-numerical values.

For dealing with the reasoning process of medical diagnosis, one can require different strategies for improving the confidence of a potential diagnosis. The Domino model defined by Das et al<sup>7,13</sup> is a mental-state model oriented to capture the mental state of an intelligent agent in order to support decision making.

Upon this background, in this paper we introduce a multi-agent approach for dealing with qualitative medical diagnosis. This approach is based on the Domino-hypothetic-deductive method. This method merges ideas from the *hypothetic-deductive* reasoning method<sup>26</sup> and the Domino model. In this setting, we argue for having different interpretation of the clinical guidelines and provide these to different intelligent agents. We introduce two kinds of agents:

- *Observer agents*: Observer agents are those which take as input a set of observations from a patient and suggest a potential disease (condition). These agents are provided by a possibilistic knowledge base and a deductive reasoning method.
- *Validating agents*: Validating agents are those which take as input a set of hypothesis which usually are the potential diseases which justify a set of observations. These agents are provided by a possibilistic knowledge base and an abductive reasoning method.

In order to lead with the reasoning process of these agents, we follow the Domino model. We will show, by considering a real clinical scenario, how our approach could support medial diagnosis in a scenario which is pervaded of uncertainty.

In general terms, we can identify, at least, the following contributions of the paper:

- (1) A new method for supporting medical diagnosis which we call the Hypothetic-Deductive-Domino (HD-D) algorithm.
- (2) A multi-agent approach designed to deal with medical qualitative diagnosis.
- (3) The introduction of basic concepts such as *possibilistic action schemas* and *plan schemas* in order to deal with medical planning.

The rest of the paper is divided as follows: in Section 2, a motivation of the introduced qualitative medical diagnosis approach and the general description of the HD-D algorithm is presented. In Section 3, some issues *w.r.t.* possibilistic knowledge bases and the interpretation of clinical guidelines are discussed. More accurately, the structures for capturing clinical guidelines in terms of deductive and abductive knowledge are presented. In Section 4, the formal definitions of the Observer and

Validating agents are presented. In Section 5, a short discussion with respect to the related work is presented. In Section 6, an outline of conclusions and future work is presented. Finally in Appendix A, some basic concepts about possibilistic logic programs are presented.

## 2. Motivation

In this section, we motivate why the integration of Possibilistic Answer Set Programming, a multi-agent agent design which follows the Domino Model (a cognitive agent model) and the hypothetic-deductive reasoning method defines a solid approach for performing medical reasoning.

### 2.1. Reasoning with incomplete and uncertain information

Logic-based methods have been explored since the first expert systems were introduced for supporting medical diagnosis. Logic-based methods usually are based on rule-based knowledge bases. Moreover, most of the rule-based systems which support medical diagnosis are based on backward chaining and forward chaining methods for giving answer to queries to their knowledge bases. However, it is known that the inferences machines based on backward chaining and forward chaining methods have limitations for dealing with *commonsense reasoning*.

Among the different knowledge representation formalisms at the forefront of research, the ones which support *non-monotonic reasoning* have emerged as a solid base for dealing with commonsense reasoning. Non-monotonic reasoning methods offer formal methods for capturing knowledge bases which are pervaded with imperfect and changing information. In the research field of non-monotonic reasoning, *Answer Set Programming* (ASP) is regarded as the state of the art<sup>3</sup>.

ASP is a pure declarative programming approach. Unlike to inference machines based on backward chaining and forward chaining methods, in the ASP's inference, the order of the program rules does not matter. The order of subgoals in a rule does not matter. Moreover the ASP's inference is able to deal with *nondeterminism* in order to deal with a sort of guessing. Therefore, ASP offers a sound approach for dealing with incomplete information by means of *negation as failure*<sup>3</sup>. Around ASP, we can find different specification languages with different purposes<sup>3</sup>. There is an extension of ASP called *Possibilistic Answer Set Programming* (P-ASP)<sup>34</sup>. P-ASP is a combination of Answer Set Programming with Possibilistic Logic<sup>9</sup> and is able to deal with incomplete and uncertain information.

As we have argued in the introduction, CGs are pervaded of ambiguities and incompleteness; however, if the knowledge captured by CGs is represented formally, it is possible to automatically reason with it. In this paper, we argue that P-ASP's language is rich enough for capturing CGs. Besides, ASP's inference machine offers different strategies in order to pursue different forms of reasoning, *e.g.*, *deductive reasoning* and *abductive reasoning*.

## 2.2. Strategies for diagnostic reasoning

According to Patel *et al.*<sup>37</sup>, we can at least identify two kinds of reasoning strategies performed by clinicians: *deductive reasoning* and *abductive reasoning*.

**Deductive reasoning:** Deductive reasoning can be seen as a basic form of medical diagnostic reasoning, forming decisions about conditions based on observations, typically as a multi-step process of refinement (*e.g.*, on basis of the set of observations  $o_1, \dots, o_n$ ,  $c$  can be assessed according to a knowledge base, *i.e.*, a formal interpretation of a clinical guideline). To make the formalization of clinical guidelines simple, the approach can be applied as in the exemplified clinical guideline<sup>1</sup>; assuming that everybody will know that assertions are not actually true from an epistemic perspective but represent the best decision at hand, knowing that this patient may be one of several exceptions. However, methods that can capture the complexity and defeasible characteristic of the generated knowledge in a patient's case are becoming increasingly attractive, to provide appropriate support in domains pervaded with *uncertainty*. Since the ultimate purpose of knowledge-based diagnostic support is to educate the less skilled physicians, the vagueness and incompleteness inherited from the evidence-based medical literature should be as explicit as possible. This enables also the provision of legitimate reasons for deviations from clinical guidelines in exceptional cases, which is highly important when evaluating the outcome of care.

**Abductive diagnostic reasoning:** Abductive diagnostic reasoning may also be seen as a form of diagnostic reasoning, where hypothesis generation and evaluation is included (*e.g.*, the set of observations  $o_1, \dots, o_n$ , can be explained as being caused by  $c$ , considering  $c$  as a hypothesis, analyzed together with a knowledge base, the formal interpretation of a clinical guideline)<sup>26</sup>. However, interpreting abductive diagnostic reasoning in this way, the knowledge base needs to contain information about diseases causing observed symptoms (causal information) in order to be able to explain the observations. Again, such statements need to capture the *uncertainty* of the knowledge domain.

Among the different scientific reasoning methods which one can find in the literature, the *hypothetic-deductive* reasoning method has been used as a problem solving method<sup>26</sup>. Hypothetic-deductive method is a very important method for testing theories or hypotheses. This method is one of the most basic methods common to all scientific disciplines including biology, physics, and chemistry. The *hypothetic-deductive* reasoning method<sup>26</sup> includes a hypothesis generation and evaluation procedure that resembles the medical diagnostic reasoning as it is done by medical professionals<sup>37</sup>. In turn each hypothesis is tested in an iterative process. The *hypothetic-deductive algorithm* can be summarized as follows:

- (1) Gather data through observations
- (2) Formulate hypothetical explanation

- (3) Deduce a consequence of explanation, predict, formulate experiment (test hypothesis)
- (4) Wait for corroboration:
  - a If corroboration, go to 3.
  - b If not corroboration, go to 2.

Step 3 differs from the abductive method, in that it involves decisions about what actions to take, e.g., do supplementary assessments to verify a hypothesis (filling in missing information or adding information to create a stronger case).

### 2.3. *Multi-Agent Model*

In clinical practice, a combination of deductive and abductive reasoning is typically seen, by *different actors* in different situations and purposes<sup>37</sup>. This motivates us to define different entities with different reasoning capabilities. In a multi-agent design, we argue for designing an intelligent agent, which is able to generate hypotheses by performing a kind of deductive reasoning. As a supplement to this agent we design another intelligent agent, which is able to validate the hypotheses from the first one by considering a kind of abductive reasoning. To divide the tasks of generating hypotheses and validating hypotheses between two different agents has at least the following advantages:

- Clinician agents with different amount of knowledge and experience can take part of a diagnostic problem solving task.
- The maintenance of the knowledge bases is distributed in space and time.
- The entry and exit of the participants which generate hypotheses or validate hypothesis is transparent.
- Allow to manage conflicts between the participants in a diagnostic problem solving process.

When viewing diagnostic reasoning as an action to be chosen among other actions by an agent, including the actions described in the algorithm and in addition to new assessments, we need a model that includes also planning and evaluation of actions.

In multi-agent literature, there are several cognitive models for designing an intelligent agent, *e.g.*, the Belief, Desire and Intention (BDI) model, and the Domino Model, which extends the BDI model<sup>7,13</sup>. The Domino Model attempts to capture human reasoning and decision making in a healthcare context. It integrates both data nodes and processes typically found in clinical practice and is suggested to form a functional base for agents in healthcare. It includes the categories: *beliefs, goals, options/hypotheses, decisions, plans* and *actions*, representing data (see Figure 1). Between these categories arrows indicate processes to generate, or utilize the information. We take a particular interest in these processes. Since the Domino model is considered as part of the state-of-the-art in describing CGs<sup>14</sup>, we take

interest in relating and comparing our approach to the Domino model.

Let us observe that the Domino model can guide the iterative process of *reasoning activities* and is useful for situating the combination of hypothetico-deductive and abductive reasoning in a context of *deliberation*, i.e., reasoning about actions. In this setting, we introduce an extended version of the hypothetico-deductive algorithm which is called *Hypothetic-Deductive-Domino*(HD-D) algorithm. This new algorithm is defined as follows:

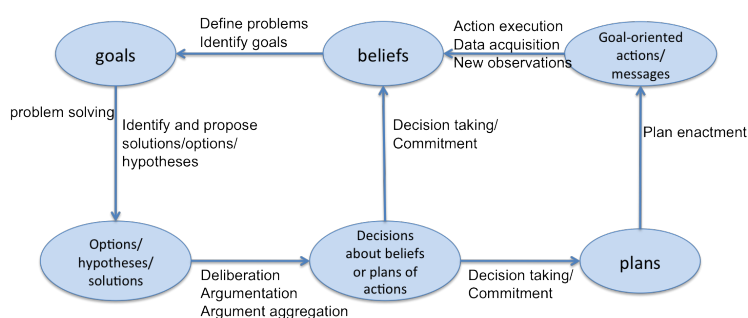


Fig. 1. Graphic representation of the Domino model.

- (1) Gather data through observations - *Investigate*
- (2) Formulate hypothetical explanation - *Diagnose*
- (3) Evaluate its strength - *Evaluate*
  - a If not satisfactory: Deduce a consequence of explanation, formulate plan of investigation (test hypothesis), and go to 1 - *Plan*
  - b If satisfactory, plan intervention - *Plan*
- (4) Intervene the situation by e.g., medication, formulate plan of investigating the effects, and go to 1 for follow-up - *Intervene*

The processes *investigate*, *diagnose*, *evaluate* and *intervene* fulfill goals in the Domino model. The corresponding task classes in the PROforma<sup>13</sup> task ontology are *Inquiry* for Investigate, and *Action* for Intervene. The evaluation task in the algorithm corresponds to the *Decision* task in the PROforma task ontology. *Planning* is considered in our model as a sub-task to the evaluation task. The outcome is decisions about diagnoses and/or which actions to perform as part of plans. This is in accordance with the Domino model, where the Plans node represents the plans to be executed<sup>13</sup>.

The algorithm now incorporates the different reasoning strategies observed in human reasoning. By defining different types of agents, which follow different strategies, we aim to capture the types of knowledge represented in different medical



sources, and enable a reasoning process which switches between strategies depending on the purpose at hand. The goal is to make the diagnostic process support transparent to medical professionals with different level of expertise, and by this providing an opportunity to develop their expertise.

In the following sections, the multi-agent approach will be presented. In this multi-agent approach:

- The agents will be provided with possibilistic knowledge bases by means of P-ASP.
- There will be two basic kinds of agents: An Observer agent, which will generate hypotheses by using a possibilistic deductive reasoning method; and a Validating agent, which will explain the hypotheses generated by the Observer agent by using a possibilistic abductive reasoning method.
- The collaboration between the Observer and Validating agents will implement the HD-D algorithm.

### 3. Deductive and abductive knowledge bases

The first issue to set up in the definition of the *Observer* and *Validating* agents is their respective knowledge bases. To this end, short declarative specifications of clinical guidelines will be introduced. These declarative specifications are defined in terms of *Possibilistic Answer Set Programming* (P-ASP). A short introduction to P-ASP is presented in Appendix A.

As it was discussed in Section 2.2, a basic premise of our approach is to consider two different reasoning models: a *deductive* and an *abductive*. Hence, two different declarative specifications of clinical guidelines will be introduced. These declarative specifications will have different aims. One knowledge base will be oriented to support deductive reasoning and the other one will be oriented to support abductive reasoning.

#### 3.1. Deductive knowledge base

We will start by introducing a possibilistic deductive knowledge base. To this end, let us remember that a deductive reasoning process is based on observations in order to infer potential diseases. Hence each rule in our deductive knowledge bases will have the following pattern:

$$uncertain\_degree : D \leftarrow Ob_1 \wedge \dots \wedge Ob_n \quad (1)$$

where *uncertain\_degree* denotes an uncertain value about the knowledge capture by the possibilistic clause, *D* denotes a medical diseases and  $Ob_i (1 \leq i \leq n)$  denotes an observation which could explain *D* (an observation can be another disease).

To illustrate a possibilistic deductive knowledge base let us consider a small summary of clinical guidelines. The clinical guidelines used in this summary are [36] and [1]. Let us introduce the following vocabulary:

*AD = Alzheimer's disease*  
*DLB = Lewy body type of dementia*  
*VaD = Vascular dementia*  
*epiMem = Episodic memory dysfunction*  
*fluctCog = Fluctuating cognition*  
*fn = Focal neurological signs*  
*prog = Progressive course*  
*radVasc = Radiology exam shows vascular signs*  
*slow = Slow, gradual onset*  
*extraPyr = Extrapyrimal symptoms*  
*visHall = Visual hallucinations*

In order to quantify the uncertain information, we have extracted the following linguistic labels describing different levels of uncertainty of assessments from the clinical guidelines:  $\mathcal{Q}_D := \{\text{confirmed}, \text{probable}, \text{possible}, \text{plausible}, \text{supported}, \text{open}\}$ . To describe their relationships, let  $<$  be a partial order such that the following set of relations holds:  $\{\text{confirmed} > \text{probable}, \text{probable} > \text{possible}, \text{confirmed} > \text{plausible}, \text{plausible} > \text{supported}, \text{possible} > \text{supported}, \text{supported} > \text{open}\}$ . Each of these labels reflects different degrees of confidence of the assessments which are expressed in CGs. Therefore, statements which are attached with the bottom of  $(<, \mathcal{Q}_D)$  expresses poor confidence about the assessments. On the other hand, assessments which are attached with the top of the lattice  $(<, \mathcal{Q}_D)$  expresses high level of confidence about the statements.

The graphic representation of  $(<, \mathcal{Q}_D)$  is presented in Figure 2. Intuitively, given  $x, y \in \mathcal{Q}_D$ , the relation  $x > y$  means that  $y$  is less certain than  $x$ .

**Example 3.1.** By considering the previous defined vocabulary and the lattice  $(<, \mathcal{Q}_D)$ , let  $P_D = ((<, \mathcal{Q}_D), N)$  be a possibilistic logic program such that  $N$  is formed by the following set of possibilistic clauses:

- (1) **probable:**  $AD \leftarrow \text{prog} \wedge \text{slow} \wedge \text{epiMem} \wedge \text{not VaD} \wedge \text{not DLB}$
- (2) **probable:**  $VaD \leftarrow \text{fn} \wedge \text{radVasc} \wedge \text{not AD} \wedge \text{not DLB}$
- (3) **probable:**  $DLB \leftarrow \text{extraPyr} \wedge \text{visHall} \wedge \text{not fn}$
- (4) **probable:**  $DLB \leftarrow \text{fluctCog} \wedge \text{visHall} \wedge \text{not fn}$
- (5) **probable:**  $DLB \leftarrow \text{fluctCog} \wedge \text{extraPyr} \wedge \text{not fn}$
- (6) **probable:**  $VaD \leftarrow \text{fn} \wedge \text{radVasc}$
- (7) **possible:**  $DLB \leftarrow \text{extraPyr} \wedge \text{fluctCog}$
- (8) **possible:**  $VaD \leftarrow \text{fn} \wedge \text{fluctCog}$
- (9) **possible:**  $DLB \leftarrow \text{fn} \wedge \text{fluctCog}$
- (10) **possible:**  $VaD \leftarrow \text{fn} \wedge \text{slow} \wedge \text{prog} \wedge \text{epiMem}$

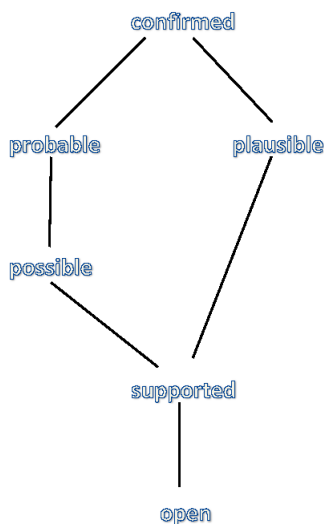


Fig. 2. Graphic representation of the lattice ( $<$ ,  $\{confirmed, probable, possible, plausible, supported, open\}$ )

- (11) **possible:**  $AD \leftarrow fn \wedge slow \wedge prog \wedge epiMem$
- (12) **possible:**  $VaD \leftarrow radVasc \wedge slow \wedge prog \wedge epiMem$
- (13) **possible:**  $AD \leftarrow radVasc \wedge slow \wedge prog \wedge epiMem$
- (14) **possible:**  $DLB \leftarrow fluctCog \wedge slow \wedge prog \wedge epiMem$
- (15) **possible:**  $AD \leftarrow fluctCog \wedge slow \wedge prog \wedge epiMem$
- (16) **possible:**  $DLB \leftarrow extraPyr \wedge slow \wedge prog \wedge epiMem$
- (17) **possible:**  $AD \leftarrow extraPyr \wedge slow \wedge prog \wedge epiMem$
- (18) **possible:**  $DLB \leftarrow visHall \wedge slow \wedge prog \wedge epiMem$
- (19) **possible:**  $AD \leftarrow visHall \wedge slow \wedge prog \wedge epiMem$
- (20) **possible:**  $DLB \leftarrow fluctCog$
- (21) **possible:**  $DLB \leftarrow visHall$
- (22) **possible:**  $DLB \leftarrow extraPyr$
- (23) **possible:**  $VaD \leftarrow fn$
- (24) **possible:**  $VaD \leftarrow radVasc$
- (25) **supported:**  $VaD \leftarrow fluctCog$
- (26) **plausible:**  $AD \leftarrow extraPyr$

Let us observe that  $P_D$  is basically capturing a possibilistic deductive knowledge base. Indeed, one can observe that each possibilistic clause which belongs to  $P_D$  follows the pattern defined in (1). Before moving on, it is worth mentioning that the consideration of linguistic labels, as the labels presented in this paper, have been explored by different authors. For instance in [23], the authors introduced quite

similar set of labels to the one presented in this paper. However, one of the main differences is that in our approach we explicitly define a partially order between the labels in order to pursuit sound inferences of the semantics of the possibilistic logic programs which is based on possibilistic logic<sup>9</sup>.

### 3.2. Abductive knowledge base

As it was discussed in Section 2.2, abductive reasoning about diagnoses in medical practice can be regarded as a process for explaining a disease in terms of symptoms. In this setting, we can re-interpret the clinical guidelines and EBM studies in order to explore what information they give on causality, *i.e.*, what we can expect to observe in an individual with a certain disease. Ideally, we would use reliable probability measures, but since these are not available or not stable over the disease progression, we use interpretations of the expressions indicating degrees of confidence. The intuitive interpretation will be:

“It is *always/likely/typically/possibly/rare* that the diagnosis  $D$  causes/explains the phenomenon  $O$  observable at some point during the disease progression”.

This motivates that each possibilistic clause in our possibilistic abductive knowledge base will have the following pattern:

$$\textit{uncertain\_degree} : Ob \leftarrow D \quad (2)$$

where *uncertain\_degree* denotes an uncertain value about the knowledge captured by the possibilistic clause,  $D$  denotes a medical diseases and  $Ob$  is an observable phenomenon. This implies to re-interpret the clinical guidelines in order to explore what information they give on causality, we identify a second lattice that captures this causality. Let  $\mathcal{Q}_C := \{\textit{always}, \textit{likely}, \textit{typically}, \textit{possibly}, \textit{rare}\}$ . Their relationships are defined as follows:  $\{\textit{always} > \textit{likely}, \textit{likely} > \textit{typically}, \textit{likely} > \textit{possibly}, \textit{possibly} > \textit{rare}, \textit{typically} > \textit{rare}\}$ . The graphic representation of this lattice is presented in Figure 3.

**Example 3.2.** By using the vocabulary introduced in Section 3.1 and the lattice  $(<, \mathcal{Q}_C)$ , let  $P_A = \langle \mathcal{Q}_C, N \rangle$  be a possibilistic logic program such that  $N$  is formed by the following set of possibilistic clauses:

- (1) **likely:**  $\textit{extraPyr} \leftarrow DLB$
- (2) **likely:**  $\textit{fluctCog} \leftarrow DLB$
- (3) **likely:**  $\textit{visHall} \leftarrow DLB$
- (4) **always:**  $\textit{fn} \leftarrow VaD$
- (5) **likely:**  $\textit{radVasc} \leftarrow VaD$
- (6) **typically:**  $\textit{fluctCog} \leftarrow VaD$
- (7) **always:**  $\textit{epiMem} \leftarrow AD$
- (8) **always:**  $\textit{slow} \leftarrow AD$

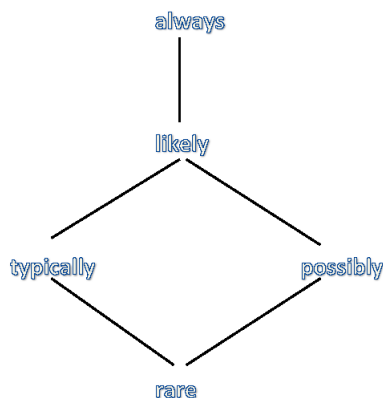


Fig. 3. Graphic representation of the lattice ( $<, \{always, likely, typically, possibly, rare\}$ )

- (9) **always:**  $prog \leftarrow AD$   
 (10) **possibly:**  $extraPyr \leftarrow AD$

Let us observe that  $P_A$  is capturing an abductive knowledge base. The expression that DLB is *likely* to cause extrapyramidal symptoms is based on the clinical knowledge that such symptoms have been observed in up to 70 % of DLB cases in EBM studies, and have been identified as one of three core symptoms for diagnosis<sup>15</sup>. The expression that AD *possibly* causes extrapyramidal symptoms is based on that such symptoms have been observed in up to 30 % of AD cases, where DLB has been excluded with reliable methods.

#### 4. Observer and Validating Agents

In this section, the ideas of *Observer* and *Validating* agents are presented. The general idea is that both *Observer* and *Validating* agents will collaborate in order to improve the quality of a potential diagnosis. Both *Observer* and *Validating* agents will be provided with a possibilistic knowledge base. Firstly, we introduce our patient Per Persson (PP), who suffers from a state of dementia, but initially, it is not clear which type of dementia that is causing the cognitive deficits. In the progressive course of a dementia disease, additional symptoms become observable and new assessments may be needed. We will exemplify a procedure of assessments accomplished by the two agents with the goal to strengthen the hypothetical diagnosis, or multi-diagnosis, to a level of confidence, which is satisfactory from a medical point of view.

#### 4.1. *Introducing Per Persson who Suffers from Dementia*

Per Persson is 87 years old and leads a very physically and mentally active life in a village where he needs to take care of his houses, forest, garden and snow in the winter time. In addition, he builds boats and furnitures. Lately it has become evident that his cognitive functions do not serve him as before. This is most visible in that he suffers from apraxia, and cannot use his tools and machines as efficiently as before. He has also difficulties remembering what he has promised to do and things that happen, which are signs of an episodic memory deficit. The difficulties have grown slowly and in a progressive way, which his wife confirms when the physician asked about this. However, the difficulties fluctuate over the course of a day. He has high blood pressure and visits the physician when he has to, but not willingly, since he thinks that health care makes people sick. So, PP does not tell the physician about things such that he has fallen a few times without reason, or that his arm does not work as it used to do, unless the physician asks directly or if his wife is given an opportunity to tell the physician about this. PP ends the meeting with the physician to go home and continue with his activities.

However, since the physician has evidence that confirms that a state of dementia is present, the question becomes *what* type of dementia is causing the cognitive deficits. The reasoning about diagnosis and additional assessments is illustrated in the following sections.

#### 4.2. *Plans*

One of the main features of the *HD-D algorithm* is the consideration of *plans* which can be considered as a sequence of *actions* in order to achieve a goal. Let us remember that the agents' goal is to improve the quality of a medical diagnosis. The effect of an action can be interpreted in several ways. In our approach, an action will be oriented to give recommendations in order to improve a medical diagnosis. In this setting, an example of an *intuitive* reading of an action can be:

*Examine focal neurological signs* in order to confirm a *probable* diagnosis of *vascular dementia*

Observe that this schema of action suggests a possible medical action, *i.e.*, to *Examine focal neurological signs*, in order to explain a hypothesis, *e.g.*, a *probable vascular dementia*. In order to capture this schema of actions, let us introduce the concept of a *possibilistic action schema*.

**Definition 4.1.** Let  $\mathcal{A}$  be a set of atoms denoting actions and  $\mathcal{S}$  be a set of possibilistic atoms. A possibilistic action schema is a tuple of the form  $\langle a, (x, \alpha) \rangle$  such that  $a \in \mathcal{A}$  and  $(x, \alpha) \in \mathcal{S}$ .

Before moving on, let us observe that a possibilistic action schema is formed by two components: an atom which denotes an action and a possibilistic atom, which is basically regarded as a goal of a possibilistic action schema. For instance, we have

talked about the action *to examine focal neurological signs* in order to confirm the presence of vascular dementia. Hence to confirm the presence of vascular dementia is *the goal* of examining neurological signs. The level of abstraction of the action to examine neurological signs is quite high in the sense that performing this action can be done by executing a plan (by plan we mean a set of actions) in order to get more observations.

The construction of possibilistic action schemas can be motivated by *Plan Schemas*. Let us consider the scenario when the confidence in a hypothetical diagnosis is too low, a *plan* containing additional phenomenon to be investigated should be created and motivated. We can define a *goal* consisting of a task and the object in focus for the task, *e.g.*, *to Examine focal neurological signs*. In addition, the goal may have a *value* representing the importance of the goal. A potential source for defining plans for investigating medical phenomenon can be medical protocols<sup>15</sup>. For instance, a possible reading of a medical Plan Scheme can be the following which will be denoted by *A*:

“If suspecting Disease  $d_a$ , then examine Phenomenon  $o_a$ , because  $o_a$  is contributing to reaching the diagnosis of the Disease  $d_a$  with the confidence level  $L$  such that  $L \in \{\text{confirmed}, \text{probable}, \text{possible}, \text{plausible}, \text{supported}\}$ ”.

Another example of a reading of a plan scheme is the following, this plan schema will be denoted by *B*:

“If suspecting Disease  $d_b$ , then examine Phenomenon  $o_b$ , because it is *always/likely/typically/possibly/rare* that the disease  $d_b$  causes/explains the phenomenon  $o_b$  observable at some point during the disease progression”.

In a more concrete way, a plan schema is defined as follows:

**Definition 4.2.** Let  $\mathcal{O}$  be a set of atoms denoting a set of observable phenomenon,  $(\mathcal{Q}, \leq)$  be a finite lattice,  $\mathcal{A}$  be a set of atoms denoting actions and  $\mathcal{D}$  be a set of atoms denoting diseases. A plan schema is a tuple of the form:  $\langle \mathcal{D}, a, \mathcal{O} \times \mathcal{Q} \rangle$  such that  $a \in \mathcal{A}$ .

In order to illustrate this definition, let us consider the following example:

**Example 4.1.** Let  $\mathcal{D} = \{AD, DLB, VaD\}$ ,  $\mathcal{A} = \{\text{examine}\}$  and  $\mathcal{O} = \{\text{epiMem}, \text{fluctCog}, \text{fn}, \text{prog}, \text{radVasc}, \text{slow}, \text{extraPyr}, \text{visHall}\}$ . Hence, the Plan schema *A* can be re-written as follows:

$$\langle \mathcal{D}, \text{examine}, \mathcal{O} \times \{\text{confirmed}, \text{probable}, \text{possible}, \text{plausible}, \text{supported}\} \rangle$$

We can observe that basically we are defining the domain of each variable of the Plan schema *A*. In the same way, one can re-write the Plan schema *B*.

A plan schema can be instantiated in order to generate a set of possibilistic action schemas. This set of possibilistic action schemas will be called *a plan*. Given a plan schema we can generate a plan by considering either a deductive knowledge base or an abductive knowledge base. In order to show how to generate possibilistic action schemas from a plan schema and a deductive knowledge base, let us introduce some notation: Given a possibilistic clause  $r$  of the form  $\alpha : d \leftarrow \mathcal{B}^+ \wedge \text{not } \mathcal{B}^-$ ,  $\text{head}(r) = d$ . Let  $P_D = \langle \langle \cdot, \mathcal{Q}_D \rangle, N \rangle$  be a possibilistic program and  $d$  be an atom.

$$\text{Head}(P_D, d) = \{r \mid r \in N, \text{head}(r) = d\}$$

$$\text{Rel.Observations}_D(P_D, d) = \{\mathcal{B}^+ \times \{\alpha\} \mid \alpha : d \leftarrow \mathcal{B}^+ \wedge \text{not } \mathcal{B}^- \in \text{Head}(P_D, d)\}$$

**Example 4.2.** Let  $P_D^1$  be the following subset of possibilistic clauses of the possibilistic program  $P_D$  which was introduced in Example 3.1:

$$\begin{aligned} \text{probable} &: \text{VaD} \leftarrow \text{fn} \wedge \text{radVasc} \\ \text{probable} &: \text{DLB} \leftarrow \text{extraPyr} \wedge \text{fluctCog} \wedge \text{not fn} \\ \text{possible} &: \text{DLB} \leftarrow \text{fluctCog} \end{aligned}$$

One can see that  $\text{Head}(P_D^1, \text{DLB}) = \{\text{probable} : \text{DLB} \leftarrow \text{extraPyr} \wedge \text{fluctCog} \wedge \text{not fn}, \text{possible} : \text{DLB} \leftarrow \text{fluctCog}\}$ . On the other hand,  $\text{Rel.Observations}_D(P_D^1, \text{DLB}) = \{(\text{extraPyr}, \text{probable}), (\text{fluctCog}, \text{probable}), (\text{fluctCog}, \text{possible})\}$ . Let us observe that  $\text{Rel.Observations}_D(P_D^1, \text{DLB})$  is basically recollecting the observable phenomenon that can suggest the presence of *Levy Body Dementia*.

By considering a plan as a set of possibilistic action schemas, a plan is defined as follows:

**Definition 4.3.** Let  $P_D = \langle \langle \cdot, \mathcal{Q}_D \rangle, N \rangle$  be a possibilistic program such that  $P_D$  is a deductive knowledge base and  $Pl = \langle \mathcal{D}, a, \mathcal{O} \times \mathcal{Q}_D \rangle$  be a plan schema. A plan *w.r.t.*  $d \in \mathcal{D}$  is defined as follows:

$$Pl_D(P_D, Pl, d) = \{ \langle a, (o, \alpha) \rangle \mid (o, \alpha) \in \text{Rel.Observations}_D(P_D, d) \text{ and } (o, \alpha) \in \mathcal{O} \times \mathcal{Q}_D \}$$

Let us continue with Example 4.2 in order to illustrate Definition 4.3.

**Example 4.3.** Let  $\text{Rel.Observations}_D(P_D^1, \text{DLB})$  be the set of possibilistic atoms defined in Example 4.2 and  $Pl$  be the plan schema introduced in Example 4.1:

Hence, a Plan *w.r.t.*  $\text{DLB}$  is:

$$\begin{aligned} Pl_D(P_D^1, Pl, \text{DLB}) = & \{ \langle \text{examine}, (\text{extraPyr}, \text{probable}) \rangle, \\ & \langle \text{examine}, (\text{fluctCog}, \text{probable}) \rangle, \\ & \langle \text{examine}, (\text{fluctCog}, \text{possible}) \rangle \} \end{aligned}$$



The intuitive reading of the plan  $Pl_D(P_D^1, Pl, DLB)$  suggests that if Lewy body dementia ( $DLB$ ) is suspected, one must explore Extrapyrimal symptoms ( $extraPyr$ ) and fluctuation cognition ( $fluctCog$ ) in order to get more evidence which could improve the confidence in a  $DLB$  diagnosis.

Like deductive knowledge bases, an abductive knowledge base can be used for instantiating plan schemas in order to generate plans. Hence, we will present some new notations. Given a possibilistic clause  $r$  of the form  $\alpha : a \leftarrow \mathcal{B}^+$ ,  $body^+(r) = \mathcal{B}^+$ . Let  $P_A = \langle \langle \cdot, \mathcal{Q}_A \rangle, N \rangle$  be a possibilistic program and  $d$  be an atom.

$$Body(P_A, d) = \{r | r \in N, body^+(r) = \{d\}\}$$

$$Rel\_Observations_A(P_A, d) = \{(o, \alpha) | \alpha : o \leftarrow \mathcal{B}^+ \in Head(P_A, d)\}$$

**Example 4.4.** Let  $P_A$  be the possibilistic program which was introduced in Example 3.2. One can see that:

$$Body(P_A, DLB) = \{likely : extraPyr \leftarrow DLB, \\ likely : fluctCog \leftarrow DLB, \\ likely : visHall \leftarrow DLB\}$$

On the other hand,

$$Rel\_Observations_A(P_A, DLB) = \{(extraPyr, likely), (fluctCog, likely), \\ (visHall, likely)\}$$

Once again, we can observe that  $Rel\_Observations_A(P_A, DLB)$  is basically recovering observable phenomenon with respect to  $DLB$ .

In the following definition, we show how to define plans from an abductive knowledge base and a plan schema.

**Definition 4.4.** Let  $P_A = \langle \langle \cdot, \mathcal{Q}_A \rangle, N \rangle$  be a possibilistic program such that  $P_A$  is an abductive knowledge base and  $Pl = \langle \mathcal{D}, a, \mathcal{O} \times \mathcal{Q}_A \rangle$  be a plan schema. A plan *w.r.t.*  $d \in \mathcal{D}$  is defined as follows:

$$Pl_A(P_A, Pl, d) = \{ \langle a, (o, \alpha) \rangle | (o, \alpha) \in Rel\_Observations_A(P_A, d) \}$$

Let us continue with Example 4.4.

**Example 4.5.** Let  $\mathcal{D} = \{AD, DLB, VaD\}$ ,  $\mathcal{A} = \{examine\}$  and  $\mathcal{O} = \{epiMem, fluctCog, fn, prog, radVasc, slow, extraPyr, visHall\}$ . Hence, let  $Pl$  be the following plan schema:

$$\langle \mathcal{D}, examine, \mathcal{O} \times \{always, likely, typically, possible, rare\} \rangle$$

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One can see that a plan *w.r.t.* *DLB* is

$$Pl_A(P_A, Pl, DLB) = \{ \langle DLB, (extraPyr, likely) \rangle, \\ \langle DLB, (fluctCog, likely) \rangle, \\ \langle DLB, (visHall, likely) \rangle \}$$

This plan suggests that if Lewy body dementia (DLB) is suspected, one must explore visual hallucinations (*visHall*), extrapyramidal symptoms and fluctuating cognition because these observable phenomenons are likely to be observed in persons with *DLB*.

### 4.3. Observer agents

Inhere, the concept of *Observer agent* will be introduced. There are four components which form an *Observer Agent*:

- I) a deductive knowledge base,
- II) set of observations,
- III) set of believes
- IV) and a set of plan schemas.

Hence, an *Observer agent* is defined as follows:

**Definition 4.5.** A *Observer agent*  $A_o$  is a tuple of the form  $\langle \Sigma, O, B, Plans \rangle$  in which

- $\Sigma$  is a deductive knowledge base,
- $O$  is a set of possibilistic atoms which are called observations,
- $B$  is a set of possibilistic atoms which are called beliefs such that the following condition holds:  $\Sigma \cup O \models B^a$  and
- $Plans$  is a set of plan schemas.

Take into account that an *Observer agent* is basically an agent which has a possibilistic knowledge base and a set of plan schemas. An *Observer agent* can get a set of observations from the world and by using a deductive inference it gets a view of the world which is captured by the set of beliefs of the world.

**Example 4.6.** Let  $A_o^1 = \langle \Sigma_1, O_1, B_1, Plans_1 \rangle$  be an *Observer agent* such that  $O_1$  is an empty set,  $Plans_1$  is a set which only contains the plan schema which was introduced in Example 4.1 and  $\Sigma_1$  is the following possibilistic program:

<sup>a</sup>See in Definition Appendix A.1 the formal definition of  $\models$ .

*probable* :  $AD \leftarrow prog \wedge slow \wedge epiMem \wedge not VaD \wedge not DLB$   
*probable* :  $VaD \leftarrow fn \wedge radVasc$   
*probable* :  $DLB \leftarrow extraPyr \wedge fluctCog \wedge not fn$   
*possible* :  $DLB \leftarrow fluctCog$   
*possible* :  $AD \leftarrow slow \wedge prog \wedge epiMem$   
*possible* :  $VaD \leftarrow fn$   
*supported* :  $VaD \leftarrow fluctCog$   
*plausible* :  $AD \leftarrow extraPyr$

One can see that given that  $O_1$  is empty; hence, the set of beliefs  $B_1$  of  $A_O^1$  is empty.

Observe that the knowledge base of  $A_O^1$  is basically capturing some knowledge for diagnosing *Alzheimer's disease* ( $AD$ ), *Vascular dementia* ( $VaD$ ) and *Lewy body type of dementia* ( $DLB$ ). Now, let us suppose that  $A_O^1$  gets the following set of observations  $O'_1$  from our patient  $PP$  according to the description in Section 4.1:

*confirmed* :  $prog \leftarrow \top$   
*confirmed* :  $slow \leftarrow \top$   
*confirmed* :  $epiMem \leftarrow \top$   
*confirmed* :  $fluctCog \leftarrow \top$

In this case, one can see that the set of beliefs of  $A_O^1$  will be the answer sets of the program  $\Sigma_1 \cup O'_1$ . In particular, this program has only one answer set which will be denoted by  $M$ . Hence  $M$  will be the set of beliefs of  $A_O^1$ . One can see that  $\{(AD, possible), (DLB, possible), (VaD, supported)\} \subseteq M$ . This means that  $A_O^1$  can believe that it is *possible* that  $PP$  could have either *Alzheimers disease* ( $AD$ ) or *Lewy body type of dementia* ( $DLB$ ). In addition,  $A_O^1$  can also believe that a diagnosis of *Vascular dementia* ( $VaD$ ) is *supported*. At this state of the diagnosis, these potential diseases are only considered as potential hypothesis which could explain the state of  $PP$ .

In terms of the Domino model, let us observe that the generation of a *hypothetic diagnosis* can be regarded as the part of the reasoning process of the Domino model. In order to achieve the second part of the Domino model, an *Observe* agent must generate a potential plan *w.r.t.* each disease which he believes is present.

**Definition 4.6.** Let  $A_O = \langle \Sigma, O, B, Plans \rangle$  be an *Observer* agent and  $Pl \in Plans$ . A plan *w.r.t.*  $(b, \alpha) \in B$  is defined as follows:

$$Plan(A_O, b) = \{ \langle a, (o, \alpha') \rangle \mid \langle a, (o, \alpha') \rangle \in Pl_D(\Sigma, Pl, b) \wedge o \notin O \}$$

Please observe that basically, a plan is suggesting to explore new observable phenomena which could *strengthen* a hypothetical diagnosis.

**Example 4.7.** Let  $A_O^1 = \langle \Sigma_1, O_1, B_1, Plans \rangle$  be the *Observer* agent introduced in Example 4.6. In Example 4.6, we saw that  $(VaD, supported) \in B_1$ . This belief of

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$A_o^1$  suggests that the vascular dementia can be present in the patient PP. Therefore,  $A_o^1$  can suggest a plan for getting more evidence with respect to the presence of vascular dementia. In this setting, we can see that:

$$Plan(A_o^1, VaD) = \{\langle examine, (fn, possible) \rangle\}$$

This means that according to  $A_o^1$ 's knowledge,  $A_o^1$  suggests to explore focal neurological signs (*fn*) in order to get more evidence about a potential vascular dementia.

#### 4.4. Validating Agents

So far we made clear that by using only a deductive knowledge, an *Observer* agent can asses a set of hypothetical diagnoses, which may be in conflict and insufficiently supported. In this subsection, the idea of *Validating* agents will be introduced. A *Validating* agent will be a specialized agent in a particular domain which will validate a potential diagnosis by using an abductive inference approach. Indeed, a *Validating* agent will take as an input the potential beliefs of an *Observer* agent.

To define the *Validating* agents, the concepts of a possibilistic abductive diagnostic problem and a possibilistic diagnosis will be defined.

Usually a (technical) diagnostic problem consists of a description of a technical system to be diagnosed, observations of the actual state of the system, and the potential reasons for effects. Hence, a *possibilistic abductive diagnostic problem* for this purpose is defined as follows:

**Definition 4.7.** A possibilistic abductive diagnostic problem (PADP) is a triple  $\langle H, \langle (\mathcal{Q}, \leq), N \rangle, O \rangle$  in which:

- $H$  is a set of possibilistic atoms such that  $\{\alpha \mid (a, \alpha) \in H\} \subseteq \mathcal{Q}$ .  $H$  is called the set of hypotheses.
- $\langle (\mathcal{Q}, \leq), N \rangle$  is a possibilistic logic program which defines an abductive knowledge base.
- $O$  is a set of atoms which are called observations.

Observe that the set of observations is a set of non-possibilistic atoms. It is expected that the possibilistic theory suggests an uncertain degree to each element of the observations.

By considering the semantics for possibilistic logic programs, a possibilistic diagnosis of a possibilistic abductive diagnostic problem is defined as follows:

**Definition 4.8.** Let  $\langle H, \langle (\mathcal{Q}, \leq), N \rangle, O \rangle$  be a possibilistic abductive diagnostic problem. A possibilistic diagnosis is a tuple  $\langle H', O_P \rangle$  such that  $H' \subseteq H$ ,  $N \cup \{\alpha : h \leftarrow \top \mid (h, \alpha) \in H'\} \models O_P$  and  $(O_P)^* = O$ .

Observe that a possibilistic diagnosis not only gives evidence for explaining a set of observations, but also it identifies an uncertainty degree for each observation.

Given that a possibilistic abductive diagnostic problem can have different diagnoses, the idea of a minimal possibilistic diagnosis is defined as follows:

**Definition 4.9.** Let  $PADP = \langle H, T_P, O \rangle$  be a possibilistic abductive diagnostic problem. A possibilistic diagnosis  $D_1 = \langle H'_1, O_{P1} \rangle$  of  $PADP$  is a minimal possibilistic diagnosis if it does not exist a diagnosis  $D_2 = \langle H'_2, O_{P2} \rangle$  of  $PADP$  such that  $(H'_2)^* \subset (H'_1)^*$ .

By having in mind, the concepts of a possibilistic abductive diagnostic problem and a possibilistic diagnosis, a *Validating agent* is defined as follows:

**Definition 4.10.** A *Validating agent*  $A_v$  is a tuple of the form  $\langle PADP, \mathcal{D}, Plans \rangle$  in which

- $PADP = \langle H, \langle (\mathcal{Q}, \leq), N \rangle, O \rangle$  is a possibilistic abductive diagnostic problem,
- $\mathcal{D}$  is a set of diagnoses *w.r.t.*  $PADP$  and
- $Plans$  is a set of plan schemas.

Consider again the running example of our patient  $PP$  introduced in Section 4.1. If we want to accomplish a HD-D reasoning process, we may proceed through the first two steps using an *Observer agent* as described in previous subsection to generate a set of hypotheses. In the third step, the hypothesis is evaluated and *possibly challenged*. In order to enrich our diagnosis, a *Validating agent* may be used for deciding upon what to observe, *e.g.*, if we have deduced the possible coexistence of  $AD$  and  $DLB$ , we may use the abductive reasoning inference to determine what features to investigate in order to create a stronger case for the hypothesis. We can also use the inference to create a stronger case for the alternative hypothesis ( $VaD$ ).

**Example 4.8.** Let us consider Example 4.7. According to agent  $A_O^1$ , there are observations which support that it is possible that the given patient could have either Alzheimer's disease ( $AD$ ) or Lewy body type dementia ( $DLB$ ) or both in a co-morbidity scenario. There is weaker support for Vascular Dementia, so a choice in this situation may be to consider only  $AD$  and  $DLB$ . Therefore, we assume that  $A_O^1$  suggests the following set of hypothesis:

$$Hypotheses = \{(AD, possible), (DLB, possible)\}$$

Let us observe that these are still too uncertain to be satisfactory for committing to a final diagnosis. The question is: can we use a *Validating agent* as a next step in the diagnosis to evaluate the hypothetical diagnoses, following the HD-D approach and find out what to do as a next step in the assessment? In order to give answer to this question, let  $PADP_1 = \langle H, T_P, O \rangle$  be a possibilistic abductive diagnostic problem such that

$$H = \{(AD, always), (DLB, always)\}$$

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$$O = \{(prog, confirmed), (slow, confirmed), (epiMem, confirmed), (fluctCog, confirmed)\}^*$$

and  $T_P$  be the abductive knowledge base  $P_A$  introduced in Example 3.2.

In order to identify the explanations (diagnoses) of  $PADP_1$ , let

$$\begin{aligned} H_1 &= \{(AD, always), (DLB, always)\} \\ H_2 &= \{(AD, always)\} \\ H_3 &= \{(DLB, always)\} \end{aligned}$$

The label *always* for potential hypotheses indicates that they always should be considered as potential explanations for, or causes of, a particular set of observations. In order to see if  $H_1$  should be considered as an explanation (defines a possibilistic diagnosis) of  $PADP$ , let  $P_{H_1}$  be  $T_P$  union the following possibilistic rules:

$$\begin{aligned} always : \quad AD &\leftarrow \top \\ always : \quad DLB &\leftarrow \top \end{aligned}$$

One can see that  $P_{H_1}$  has a unique possible answer set:

$$M_{H_1} = \{(extraPyr, likely), (fluctCog, likely), (visHall, likely), (epiMem, always), (slow, always), (prog, always), (DLB, always), (AD, always)\}.$$

Let  $O_{H_1} = \{(fluctCog, likely), (prog, always), (epiMem, always), (slow, always)\}$ . Since  $O_{H_1} \subseteq M_{H_1}$  and  $O_{H_1}^* = O$ ,  $\langle H_1, O_{H_1} \rangle$  is a possibilistic diagnosis of  $PADP_1$ .

Let us check if  $H_2$  defines a possibilistic diagnosis of  $PADP_1$ . Hence, let  $P_{H_2}$  be  $T_P$  union the following possibilistic rule:

$$always : \quad AD \leftarrow \top$$

$P_{H_2}$  has a unique possible answer set:

$$M_{H_2} = \{(epiMem, always), (slow, always), (prog, always), (extraPyr, likely), (DLB, always)\}$$

Since  $O \not\subseteq M_{H_2}^*$ ,  $H_2$  does not define a possibilistic diagnosis of  $PADP$ .

Now let us check if  $H_3$  defines a possibilistic diagnosis of  $PADP$ . So let  $P_{H_3}$  be  $T_P$  union the following possibilistic rule:

$$always : \quad DLB \leftarrow \top$$

$P_{H_3}$  has a unique possible answer set:

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$$M_{H_3} = \{(extraPyr, likely), (fluctCog, likely), (visHall, likely), (DLB, always)\}$$

In this case, we can see again that  $O \not\subseteq M_{H_3}^*$ , this means that  $H_3$  does not define a possibilistic diagnosis of  $PADP$ .

Hence, we can see that  $PADP$  has a unique diagnosis:  $\langle H_1, O_{H_1} \rangle$ . Therefore, a Validating agent  $A_v^1$  can be instantiated in the following tuple:

$$A_v^1 = \langle PADP_1, \{\langle H_1, O_{H_1} \rangle\}, \{Pl\} \rangle$$

where  $Pl$  is the plan schema which was introduced in Example 4.5. One can observe that  $A_v^1$  has a unique minimal possibilistic diagnosis *w.r.t.*  $PADP_1$  which is  $\langle H_1, O_{H_1} \rangle$ . Hence, the Validating agent  $A_v^1$  can conclude that both  $AD$  and  $DLB$  can be present in Patient  $PP$ . However, since more information is needed, the Validating agent's knowledge can also be used to identify the next step in the diagnosis process. In this sense, a plan of actions can be required.

Like an Observer agent, a Validating agent follows the Domino model reasoning process. Hence, a Validating agent can suggest a plan *w.r.t.* each disease that he can explain. At this point the Validating agent does not necessarily have to suggest a plan that targets one of the two hypotheses with the stronger level of confidence. Instead, it can target the alternative hypothesis, due to the fact that the supporting evidence indicates that it should be taken into consideration, and due to the fact that the potential plan generated by the agent targets the strongest likelihood to be successful.

**Definition 4.11.** Let  $A_a = \langle PADP, \mathcal{D}, Plans \rangle$  be a Validating agent such that  $PADP = \langle H, P_A, O \rangle$  is a possibilistic abductive diagnostic problem and  $Pl \in Plans$ . A plan *w.r.t.*  $(b, \alpha) \in H$  such that  $\langle H, O \rangle \in \mathcal{D}$

$$Pl_A(A_a, b) = \{\langle a, (o, \alpha) \rangle \mid \langle a, (o, \alpha) \rangle \in Pl_A(P_A, Pl, d), o \notin O\}$$

**Example 4.9.** Let  $A_a^1 \langle PADP, \mathcal{D}, Plans \rangle$  be the Validating agent introduced in Example 4.8. One can see that:

$$Pl_A(A_a^1, AD) = \{\langle examine, (extraPyr, possibly) \rangle\}$$

$$Pl_A(A_a^1, DLB) = \{\langle examine, (extraPyr, likely) \rangle, \langle examine, (visHall, likely) \rangle\}$$

$$Pl_A(A_a^1, VaD) = \{\langle examine, (fn, always) \rangle\}$$

$Pl_A(A_a^1, AD)$  suggests that one can explore Extrapyramidal symptoms (*ExtraPyr*) in order to get a little bit more confidence about the presence of Alzheimer's disease. On the other hand, one can explore Extrapyramidal symptoms (*ExtraPyr*) and Visual Hallucinations (*visHall*) in order to get more evidence about the presence of Lewy body dementia. On the third hand, one can explore focal neurological signs in order to get even more reliable evidence about vascular dementia.

Which plan to select depends on the strategy the agent may apply. The agent may have a strategy to target the diagnosis with the highest support in the current situation, which would be AD and DLB. Or it can select the plan that gives most reliable information, which is the plan about VaD (*always*). Let us assume it strives for reliability (and not a quick jump to a conclusion), so it suggests the plan targeting focal neurological signs, which always should be present in vascular dementia.

On the other hand, the Observer agent may have other reasons to target actions. The following plans can be generated, partly exemplified in Example 4.7:

$$Plan(A_o^1, VaD) = \{\langle examine, (fn, probable) \rangle, \langle examine, (radVasc, probable) \rangle\}$$

$$Plan(A_o^1, AD) = \{\langle examine, (ExtraPyr, plausible) \rangle\}$$

$$Plan(A_o^1, DLB) = \{\langle examine, (ExtraPyr, probable) \rangle\}$$

Let us assume that the Observer agent prefers high probability and suggests the plan targeting *DLB* since radiology examinations are not currently available. In our example we assume that they are cooperative, so that they agree on the investigation of extrapyramidal symptoms. Going back to our patient case Per Person, PP, the examination of motor functions to detect extrapyramidal symptoms reveals that PP:s motor dysfunction is not extrapyramidal symptoms (*parkinsonism*), but focal neurological signs (*fn*) indicating a vascular cause. As a consequence, the support for *DLB* is weakened and excluded as a potential diagnosis, and the support for vascular dementia is stronger, leading to the following updated diagnostic hypotheses

$$Hypotheses = \{(AD, possible), (VaD, possible)\}$$

At this point, the next round in the domino model would lead to again propose radiology examination. In case this can be accomplished, it would also reveal focal neurological signs corresponding to re-occurrent vascular lesions. However, as long as no radiology examination is done, the co-existence of AD and VaD is the most reliable diagnosis given the available knowledge.



## 5. Related Work

The development of formal methods for supporting medical diagnosis has a long standing tradition since the introduction of the first AI-based reasoning methods<sup>39</sup>. Given the nature of EBM knowledge is not strange that the probabilistic-based methods are the ones which predominate in decision support systems in the medical domain<sup>11,12,33</sup>. Indeed, in the state of the art we can find several knowledge-based systems based on probabilistic methods<sup>42,22</sup>. However, it is known that probabilistic methods are not the best one for performing *commonsense reasoning*<sup>18,10,29</sup>. Cognitive psychology researchers argue that expert and novice doctors use different mental strategies for coming out with a diagnosis<sup>6</sup>. According to Coderre *et al.*<sup>6</sup> there are three different diagnostic reasoning strategies which are performed by doctors: *hypothetic-deductive strategy*, *scheme-inductive problem solving strategy* and *pattern-recognition strategy*. From these methods, the hypothetic-deductive strategy has showed to be a flexible strategy for supporting the implementation of decision support systems based on logic-based methods in the medical domain<sup>26</sup>. In this setting the approach presented in this paper extends the ideas introduced by Lucas<sup>26</sup> by means of the extension of the *hypothetic-deductive algorithm*.

A primary issue for implementing cognitive strategies is the representation of EBM knowledge. EBM knowledge is the base for the development of CGs and treatment protocols. These are documents offering a description of steps and considerations that must be taken into account by health-care professionals when managing a disease in a patient, to avoid substandard practices or outcomes<sup>19</sup>. However, the work done on developing and distributing CGs and treatment protocols outweighs the efforts on guaranteeing their quality. In medicine the goal for diagnostic reasoning is assessing causes of observed conditions in order to make informed choices about treatment. Clinical guides promote the use of consistent terminology and to be able to systematically select similar treatment strategies. The knowledge about causes of diseases is preferably created in randomized clinical trials, generating EBM knowledge. This knowledge is based on probabilities, *e.g.*, if there is evidence that a certain disease is causing a given observed or measured phenomenon in a proportion of all cases of this disease. In addition, knowledge about the proportion of the manifested phenomenon in the total population is needed, including subjects not having the disease in order to assess the diagnostic value of the observation. If the observation has a high diagnostic value (*i.e.*, seen in a large proportion of cases with the disease and in a low proportion of cases without the disease) it is typically included in medical guidelines for diagnosis.

CGs are structures that contain general descriptions, defined by health care organizations, of the way in which a particular pathology should be treated<sup>21</sup>. A CG, when well-developed, is a highly matured therapeutic plan that compiles optimal practices for treating patients in a well-defined medical syntax. Thus, the adoption of CGs is a promising way for standardizing and improving health care practices as has been shown for instance by Mersmann and Dojat<sup>30</sup>. In our approach, we

consider CGs as sources of the knowledge bases of both Observer and Validating agents.

Considering the increasing cost of medical services in the healthcare domain, the efficient usage/management of medical resources has become a critical issue. The computerization of CGs using a multi-agent system framework requires the agents to work in coordination over the complex activities defined in any CG<sup>41</sup>. CGs facilitate clinical reasoning, because a guideline can be adapted, tailored and applied to different clinical situations. CGs help physicians, specially novices physicians, to use the clinical knowledge about the patient at the appropriate point of his/her care provision tasks.

There is the need for specific ontologies to serve as a basis for establishing a common understanding of the healthcare domain concepts/terminology, among disparate agents, *i.e.* built by different users with different objective<sup>20</sup>. Sharing of such understanding enables the co-ordinating agents to interpret and implement the CG correctly and thereby giving better support to the users.

One way to use formal methods in the context of clinical guidelines is to automatically verify whether or not a clinical guideline fulfills particular properties, such as whether it complies with quality indicators as proposed by health-care professionals<sup>28</sup>. Lucas has shown that the theory of abductive diagnosis can be taken as a foundation for the formalization of quality criteria of a clinical guideline<sup>27</sup> and that these can be verified using (interactive) program verification techniques<sup>19</sup>.

Beyond medical diagnostic reasoning, logic-based methods have been used by healthcare systems<sup>2,5,32,35</sup> in order to provide different services related to a person's daily activities. For instance, there are proposals which use logic-based methods in order to support *activity recognition*<sup>2,5,35</sup>. There are other proposals also based on logic-based methods which aims to monitoring the patients' activities, health and well-being in their homes in order to support health caregivers<sup>32</sup>. One can see that proposals as the one suggested by Mileo *et al.*<sup>32</sup> can take advantage of the proposal of this paper in order to provide services of medical diagnosis. It is worth mentioning that *medical adherence*<sup>8</sup> is one of the main problems in health care. Hence, the integration of monitorization of patients and medical diagnosis methods (as the one presented in this paper) can play a fundamental role in order to confront medical adherence.

## 6. Conclusions and future work

In this paper we introduced a multi-agent approach for dealing with qualitative medical diagnosis. This approach is based on the HD-D method. This method merges ideas from the *hypothetic-deductive* reasoning method and the Domino model. In this setting, we argue for having different interpretations of the CGs and EBM knowledge, and provide these to different intelligent agents.

We have argued that possibilistic logic programs define a rich approach for capturing real medical knowledge. Indeed, it seems that the introduced qualitative

diagnosis approach (see §3-§4) has practical applications in medical diagnosis since it combines different strategies in a diagnostic reasoning process in a similar way as the human approaches the task. In this way the human (*i.e.*, expert or novice clinician) may gain support tailored to his or her need in a collaborative and transparent reasoning and problem-solving process.

The consideration of intelligent systems, which could suggest and/or validate a potential disease could improve the quality of a medical diagnosis, which is done by a novice clinician. Hence, the consideration of intelligent systems which could follow the approach of *Observer* and *Validating* agents can aid in early detection of mental diseases.

Our approach allows a first step towards the use of a *manageable* and sound formalism to ease the medical diagnosis procedure. It opens opportunities for decision support, clinical workflow and other knowledge management technologies in patient care and clinical research. As shown in §4 it allows to represent several reasoning procedures and, if necessary, to combine those to allow stronger diagnosis procedures. Also, our formalism may help in capturing the dynamic nature of medical knowledge. Hence, it allows the *explanation* of the reasoning procedures.

In general terms, the following are the identified contributions of the paper:

- (1) A new method for supporting medical diagnosis, which we call the Hypothetic-Deductive-Domino algorithm §2.3.
- (2) A multi-agent approach designed to deal with qualitative diagnostics in clinical practice §4.
- (3) The introduction of basic concepts such as *possibilistic action schemas* and *plan schemas* in order to capture medical protocols §4.

### 6.1. *Future Work*

As future work there are several topics which will be explored. The first topic is to allow agents to disagree. In current proposal, the *Observer* agents generate hypotheses and the *Validating* agents suggests different justifications of the hypotheses suggested by the *Observer* agents; however, they are not allowed to disagree. To allow disagreements between agents will represent a step forward to the current proposal in order to deal with *defeasible information*, which is present in CGs.

The second main topic in our future work is to have a complete implementation of the suggested approach. Currently, we already have specifications of CGs, which are consulted by deductive reasoning machines<sup>24</sup>. These specifications are managed by a kind of *Observer* agents. Therefore, we will extend our current implementation by adding *Validating* agents.

The third main topic in our future work will be the integration of our diagnosis tools and *intervention* tools. Improving the diagnostic process is the first step in the holistic management of patients, aiming for patient-centric healthcare. The second step includes the *interventions*, *management* and *continuous followup* on the disease progression. The purpose of intervention is of course primarily to cure, if possible.

However, for most dementia diseases there is no cure, instead the goal is to minimize the effects of the disease, by means of compensation for lack of ability and treating the symptoms. Key to providing optimal intervention to an individual, is knowledge about performance of daily activities and the individual's mental condition, and how these changes over time. Preventing unnecessary decrease in ability is central, which could be caused by falls, exposure to stress factors, or other risk factors. These assessments for diagnosis and intervention are currently done by health professionals partly based on limited amount of observations and clinical interviews with the individual and informants. The challenge for a knowledge-based support system is to combine the diagnostic routine (for *e.g.*, disease, mental state, activity performance, *etc.*) with decisions and deployment of tailored interventions, and assess the outcome continuously for providing timely adjustments of the support in a daily life situation.

The use of formal logic reasoning has the advantage that it can be integrated in a context which includes *e.g.*, ubiquitous methods and sources for collecting information about daily activities and their performance. This is currently done as part of our ongoing work where three approaches to activity recognition are combined, representing three sources of information based on observations of daily activities<sup>25</sup>. In this setting, we are exploring methods for monitoring and supporting people with *mild cognitive impairments*<sup>17</sup> and people presenting *social withdrawal and mild depression*<sup>16</sup>. To this end, we have been using the sensors, which are provided by smart phones as one approach. Therefore our third main topic in our future work will be the integration of our diagnosis tools and intervention tools. It is worth mentioning that there are context-aware activity monitoring systems which are based on formal methods such as ASP for supporting activity monitoring<sup>31</sup>. Therefore, the consideration of a multi-agent approach based on our design of Observer and Validating agents can improve the management of the uncertain information which is present in human activity monitoring. Finally, it is worth mentioning that *medical adherence*<sup>8</sup> is one of the main problems in health care. Hence, the integration of monitorization of patients and medical diagnosis methods (as the one presented in this paper) can play a fundamental role in order to improve medical adherence. In this context, logic-based methods seem as strong candidates for building sound health care systems.

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### Appendix A. Possibilistic Answer Set Programming

In this appendix, we introduce some basic concepts of logic programs in the context of Possibilistic Logic Programming, for more details see <sup>34</sup>. We start introducing the basic syntax of standard disjunctive logic programs.

An extended disjunctive clause,  $C$ , is denoted as:

$$a_1 \vee \dots \vee a_m \leftarrow a_{m+1}, \dots, a_j, \text{not } a_{j+1}, \dots, \text{not } a_n$$

where  $m \geq 0$ ,  $n \geq 0$ , each  $a_i$  is an atom. When  $n = 0 \wedge m > 0$  the clause is an abbreviation of  $a_1 \vee \dots \vee a_m$ . When  $m = 0$  the clause is an abbreviation of  $\perp \leftarrow a_1, \dots, a_n$  such that  $\perp$  is the proposition symbol that always evaluates to false. Clauses of this form are called constraints (the rest, non-constraint clauses). An extended disjunctive program  $P$  is a finite set of extended disjunctive clauses. By  $\mathcal{L}_P$ , we denote the set of atoms in the language of  $P$ .

We denote an extended disjunctive clause  $C$  by  $\mathcal{A} \leftarrow \mathcal{B}^+, \text{not } \mathcal{B}^-$ , where  $\mathcal{A}$  contains all the head atoms,  $\mathcal{B}^+$  contains all the positive body atoms and  $\mathcal{B}^-$  contains all the negative body atoms. When  $\mathcal{B}^- = \emptyset$ , the clause is called positive disjunctive clause. A set of positive disjunctive clauses is called a positive disjunctive logic program. When  $\mathcal{A}$  is a singleton set, the clause can be regarded as a normal clause. A normal logic program is a finite set of normal clauses. Finally, when  $\mathcal{A}$  is a singleton set and  $\mathcal{B}^- = \emptyset$ , the clause can be also regarded as a definite clause. A finite set of definite clauses is called a definite logic program.

Now we are going to introduce of possibilistic disjunctive logic programs.

A *possibilistic atom* is a pair  $p = (a, q) \in \mathcal{A} \times \mathcal{Q}$ , in which  $\mathcal{A}$  is a finite set of atoms and  $(\mathcal{Q}, \leq)$  is a lattice. The projection  $*$  to a possibilistic atom  $p$  is defined as follows:  $p^* = a$ . Also given a set of possibilistic atoms  $S$ ,  $*$  over  $S$  is defined as follows:  $S^* = \{p^* | p \in S\}$ .

Let  $(\mathcal{Q}, \leq)$  be a lattice. A possibilistic disjunctive clause  $R$  is of the form:

$$\alpha : a_1 \vee \dots \vee a_m \leftarrow a_{m+1} \wedge \dots \wedge a_j \wedge \text{not } a_{j+1} \wedge \dots \wedge \text{not } a_n$$

in which  $\alpha \in \mathcal{Q}$  and each  $a_i (1 \leq i \leq n)$  is an atom. Sometimes a possibilistic disjunctive clause  $R$  is denoted by  $\alpha : \mathcal{A} \leftarrow \mathcal{B}^+ \wedge \text{not } \mathcal{B}^-$ .

The projection  $*$  for a possibilistic clause is  $R^* = \mathcal{A} \leftarrow \mathcal{B}^+ \wedge \text{not } \mathcal{B}^-$ . On the other hand, the projection  $n$  for a possibilistic clause is  $n(R) = \alpha$ . This projection denotes the degree of necessity captured by the certainty level of the information described by  $R$ .

“ $\alpha$  is not a probability (like it is in probability theory), but it induces a *certainty* (or *confidence*) scale. This value is determined by the expert providing the knowledge base”

A possibilistic constraint  $C$  is of the form:

$$\top_{\mathcal{Q}} : \leftarrow \mathcal{B}^+ \wedge \text{not } \mathcal{B}^-$$

in which  $\top_{\mathcal{Q}}$  is the top of the lattice  $(\mathcal{Q}, \leq)$ . The projection  $*$  for a possibilistic constraint  $C$  is:  $C^* = \leftarrow \mathcal{B}^+ \wedge \text{not } \mathcal{B}^-$ .

A possibilistic disjunctive logic program  $P$  is a tuple of the form  $\langle (\mathcal{Q}, \leq), N \rangle$ , in which  $N$  is a finite set of possibilistic disjunctive clauses and possibilistic constraints. The generalization of  $*$  over  $P$  is as follows:  $P^* = \{r^* | r \in N\}$ . Notice that  $P^*$  is an extended disjunctive program. When  $P^*$  is a normal program,  $P$  is called a possibilistic normal program. Also, when  $P^*$  is a positive disjunctive program,  $P$  is called a possibilistic positive logic program and so on. A given set of possibilistic disjunctive clauses  $\{\gamma, \dots, \gamma\}$  is also represented as  $\{\gamma; \dots; \gamma\}$ .

In the following definition a particular notation of the inference of the possibilistic answer set semantics is introduced. To this end, let us denote by  $SEM^{poss}$  the possibilistic logic programming semantics introduced in [34].

**Definition Appendix A.1.** Let  $P = \langle (\mathcal{Q}, \leq), N \rangle$  be a possibilistic logic program and  $S$  be a set of possibilistic atoms.  $P \models S$  holds if there exists a possibilistic answer set  $M \in SEM^{poss}(P)$  such that  $S \subseteq M$ .