Quality Checking of Medical Guidelines Using Interval Temporal Logics: A Case-Study

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Abstract. Computer-based decision support in health-care is becoming more and more important in recent years. *Clinical Practise Guidelines* are documents supporting health-care professionals in managing a disease in a patient, in order to avoid non-standard practices or outcomes. In this paper, we consider the problem of formalizing a guideline in a logical language. The target language is an interval-based temporal logic interpreted over natural numbers, namely the Propositional Neighborhood Logic, which has been shown to be expressive enough for our objective, and for which the satisfiability problem has been shown to be decidable. A case-study of a real guideline is presented.

1 Introduction

Computer-based decision support in health-care is becoming more and more important in recent years. *Clinical Practise Guidelines* (CPGs from now on) are documents supporting health-care professionals in managing a disease in a patient, in order to avoid non-standard practices or outcomes. Such guidelines are sets of recommendations and/or rules developed in a systematic way designed in order to help professionals and patients in the decision-making process concerning an appropriate health-care pathway [7]. The correct use of CPGs treating patients can be considered a good quality indicator in the health-care process; one of the main problems is how to (systematically) measure the correct application of a CPG on a specific patient.

Guidelines can be seen, from a computer scientist point of view, as a highly structured real-world example of document amenable to formalization for (semi)-automatic verification. Following [6], it is possible to identify four areas in the process of developing guideline-based decision support systems: a) modeling and representation; b) adquisition; c) verification and testing, and d) execution. Implementing guidelines in computer-based decision support systems promises to

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improve acceptance and application of guidelines in daily practice because the actions and observations of health-care workers are monitored and advises are produced whenever a guideline is not followed.

There are two main approaches for implementing guidelines: 1) developing and using meta-languages specifically designed for guidelines, and carrying some sort of decision support system, and 2) formalizing some (usually temporal) general properties that a certain guideline should meet, and investigating whether this is the case or not. As for the first approach, good example are PROForma [8], Asbru [18], and GLIF [15]. As for the second one, for example in [16], Panzarasa and Stefanelli describe the implementation of a workflow management system for an actual guideline; other possible approaches are those by Hederman and Smutek [12], Dazzi et.al. [5], and the temporal similarity querying method for clinical workflows proposed by Combi et.al. [4]. Hommersom, Lucas, and Balser [13,14] observed how temporal logics are particularly adapted for the formalization of CPGs, due to the importance of the temporal component in the event-sequence described by a guideline. In [13,14], the authors have centered themselves in a particularly simple temporal logic, that is, the point-based temporal logic of linear time called LTL[F,P] (see, for example, the book [9]). Such a formalism presents certain advantages, since its syntax is very intuitive, and the logic has very good computational properties. On the other hand, the use of LTL[F,P] can be considered quite limitative, because 1) LTL[F,P] is not very expressive, 2) events such as the administration of a certain drug and its effects must be considered as *instantaneous*, and 3) in a point-based logic, no duration or overlapping of events can be formalized. In [17] it has been advocated the use of interval-based temporal logic for the formalization of guidelines, focusing on possible extensions of existing propositional languages with metric features.

In this paper, in the line of [17], we consider Propositional Interval Neighborhood Logic [3,10] (PNL for short), and we show how this logic can be used to formalize a CPG. We consider a complete case-study, namely a Spanish Clinical Guideline for No-Traumatic Subarachnoid Hemorrhage (HSA from now on), based on [19], and we show a possible translation into PNL of the time-related medical events and treatments. Then, we illustrate how it is possible to take advantage from such a formalization and from the recent advances on automatic deductive methods for PNL.

2 Interval Temporal Logics: Choices, Advantages and Disadvantages

Interval temporal logics are based on interval structures over linearly ordered domains, where time intervals, rather than time instants, are the primitive ontological entities. Interval reasoning arises naturally in various fields of artificial intelligence, such as theories of actions and change, natural language analysis and processing, constraint satisfaction problems, etc. Temporal logics with interval-based semantics have also been proposed as a useful formalism for specification and verification of hardware and of real-time systems. The variety of relations between intervals in linear orders was first studied systematically by Allen [1], who also proposed their use in systems for time management and planning. Thus, the relevance of interval temporal logics in many areas of artificial intelligence is widely recognized. Interval temporal logics employ modal operators corresponding to various relations between intervals, in particular the 13 different binary relations (on linear orders) known as Allen's relations. In [11], Halpern and Shoham introduced a modal logic for reasoning about interval structures, hereafter denoted by HS, with modal operators corresponding to Allen's interval relations. Formulas of HS are evaluated at intervals, i.e., pairs of points, and consequently, they translate into binary relations in interval models. Thus, the satisfiability problem of interval logics corresponds to the satisfiability problem of dyadic first-order logic over linear orders, causing its complex and generally bad computational behavior, where undecidability is the common case, and decidability is usually achieved by imposing strong restrictions on the interval-based semantics, which often essentially reduce it to a point-based one.

However, a renewed interest in the area has been recently stimulated by the discovery of some interesting decidable fragments of HS [2,3]. In the rest of this section, we give a general view of Propositional Neighborhood Logic, which constitutes an important exception in temporal logics for intervals, being decidable (in NEXPTIME) and since it has been developed a terminating deduction method for it.

2.1 Propositional Neighborhood Logic

The syntax and semantics of propositional neighborhood logic (PNL for short), interpreted over linear orders, are defined as follows. Let $\mathbb{D} = \langle D, < \rangle$ be a linearly ordered set (which, in this work, we can suppose as a prefix of $\mathbb{N}$; decidability of PNL over the class of all linearly ordered sets, and over the class of all dense linearly ordered sets have been proved as well.). An *interval* over $\mathbb{D}$ is an ordered pair $[a, b]$, where $a, b \in D$ and $a \leq b$. We write $\mathbb{I}(\mathbb{D})$ for the set of all intervals on a given linearly ordered set. The language of *Full Propositional Neighborhood Logic* (PNL) consists of a set $\mathcal{AP}$ of propositional letters, the propositional connectives $\neg, \vee$, the modal constant π, and the modal operators $\langle A \rangle$ and $\langle \overline{A} \rangle$. The other propositional connectives, as well as the logical constants $\top$ (*true*) and $\bot$ (*false*) and the dual modal operators $[A]$ and $[\overline{A}]$, are defined as usual. *Formulas* of PNL, denoted by $\varphi, \psi, \ldots$, are recursively defined by the following grammar:

$$\varphi ::= p \mid \neg\varphi \mid \varphi \vee \phi \mid \langle A \rangle \varphi \mid \langle \overline{A} \rangle \varphi.$$

The semantics of PNL is given in terms of *interval models* $\mathbf{M} = \langle \mathbb{I}(\mathbb{D}), V \rangle$. The *valuation function* $V : \mathcal{AP} \mapsto 2^{\mathbb{I}(\mathbb{D})}$ assigns to every propositional variable p the set of intervals $V(p)$ over which p holds. The *truth relation* of a formula at a given interval in a model $\mathbf{M}$ is defined by structural induction on formulas:

- $\mathbf{M}, [a, b] \Vdash p$ iff $[a, b] \in V(p)$, for all $p \in \mathcal{AP}$;
- $\mathbf{M}, [a, b] \Vdash \neg\psi$ iff it is not the case that $\mathbf{M}, [a, b] \Vdash \psi$;

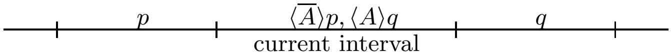

Fig. 1. A pictorial representation of PNL modalities

- $\mathbf{M}, [a, b] \Vdash \varphi \vee \psi$ iff $\mathbf{M}, [a, b] \Vdash \varphi$ or $\mathbf{M}, [a, b] \Vdash \psi$;
- $\mathbf{M}, [a, b] \Vdash \langle A \rangle \psi$ iff there exists c such that $c > b$ and $\mathbf{M}, [b, c] \Vdash \psi$;
- $\mathbf{M}, [a, b] \Vdash \langle \overline{A} \rangle \psi$ iff there exists c such that $c < a$ and $\mathbf{M}, [c, a] \Vdash \psi$.

A formula is *satisfiable* if it is true over some interval in some interval model (for the respective language) and it is *valid* if it is true over every interval in every interval model.

As shown in [10], PNL is powerful enough to express interesting temporal properties, e.g., they allow one to constrain the structure of the underlying linear ordering. In particular, in this language one can express the *universal* operator[1] (denoted here by $[U]\psi$), and thus simulate *nominals* (denoted by $N(p)$), where p is a distinguished propositional variable; recall that $\mathbf{M}, [a, b] \models N(p)$ if and only if $\mathbf{M}, [a, b] \models p$ and there is no interval $[c, d] \neq [a, b]$ such that $\mathbf{M}, [c, d] \models p$.

3 A Case Study: Translating a Spanish Clinical Guideline for Non-Traumatic Subarachnoid Hemorrhage into PNL

The main objective of the present paper is to show that PNL is powerful enough to express natural language specifications of CPGs under suitable assumptions. To this end, we consider a Spanish Clinical Guideline for Non-Traumatic Subarachnoid Hemorrhage, based on [19].

We will need a first phase of abstraction, which must be approved by a medical expert; as a second phase, we will translate the result into well-formed formulas of PNL. We will respect the ordering given by the CPG, and we will proceed to the first phase paragraph-by-paragraph.

Temporal and qualitative abstraction. An important aspect of the natural language is the capability to represent qualitative and temporal abstractions. For example, consider the sentence "*The patient had abnormally high serum creatinine after taking ACE inhibitors for less than two weeks*". The portion "*abnormally high serum creatinine*" can be considered as a qualitative abstraction indicating, say, "*creatinine greater than 2 mg/dl*", while "*for less than two weeks*" can be considered as a temporal abstraction, indicating, say, for a time less than 15 days, or less than 360 hours. Sentences of this type are very common in CPGs, and their interpretation often requires additional knowledge from an expert. Throughout this paper, we will indicate this kind of assumptions as parameters that can be modified by a physician.

[1] In this paper, we do not consider point-intervals.

Simulating the clock. PNL does not offer any metrical or quantitative feature. Nevertheless, thanks to the universal operator and nominals, we can make use of very weak form of quantitative constraint. Under the assumption that any given medical event and treatment can be considered interesting for a bounded period of time (which depends on the particular medical condition we consider), we can simulate the clock at a certain given granularity (i.e., at the level of hours, days, seconds...), and later use this clock in order to formalize medical requirements. In our case-study, for example, a quick analysis of the CPG makes clear that a good choice is to fix the granularity to the level of hours. So, let $T = \{t_1, t_2, \ldots\}$ be a *finite* set of propositional variables, each one of them is intended to represent respectively the first, second, etc., time-unit of the sequence of medical events. These propositional letters will to form an uninterrupted sequence, and no t_i can overlap t_j when $i \neq j$. Since this requirement cannot be expressed in a general form, we use nominals in order to represent (the initial part of) a finite model, as follows:

$$Time^k_{hours} = \langle A\rangle(N(t_1) \wedge \langle A\rangle(N(t_2) \wedge \langle A\rangle(N(t_3) \ldots \langle A\rangle N(t_k) \ldots))). \qquad (1)$$

It is also convenient to use special propositional letter t to indicate any of the time-unit, so:

$$[U](\bigvee_{i=1}^{k} t_i \leftrightarrow t), \qquad (2)$$

Definition 1. *Let* $\mathbf{M}$ *be any model such that, for some interval* $[a, b]$*,* $\mathbf{M}, [a, b] \Vdash$ *(1)* $\wedge$ *(2). Then, we can identify a sequence* $b = b_0 < b_1 < b_2 < \ldots b_k$ *of points such that, for each* i*,* b_i *begins a t-interval; we call such a sequence a* time-sequence*.*

Now, if we suppose that each time-unit corresponds, in the real world, to, let us say, 1 hour, the most effective way to use the above framework is to assume that medical events of interests are all above the 1-hour granularity level; clearly, this is a temporal abstraction. So, we assume:

$$\bigwedge_{p \in M} [U](p \rightarrow (\langle A\rangle t \vee [A]\bot) \wedge (\langle \overline{A}\rangle t \vee [\overline{A}]\bot)), \qquad (3)$$

where M is the set of all medical events of interest (propositional letters) used in the formalization.

A useful shortcut that can be used in this framework is the following one:

$$MinTime(l, p) = \langle A\rangle p \vee \underbrace{\langle A\rangle(t \wedge \langle A\rangle\top \wedge \langle A\rangle(p \vee ((\langle A\rangle t \wedge \langle A\rangle\top \wedge \langle A\rangle \ldots)))}_{l},$$

which, for $l \in \mathbb{N}$, makes sure that no more than l time units (assuming that the model is long enough) pass before the next occurrence of p.

Proposition 1. *Let* $\mathbf{M} = \langle \mathbb{I}(\mathbb{D}), V\rangle$ *be any model based on (a prefix of)* $\mathbb{N}$ *such that, for some interval* $[a, b]$*,* $\mathbf{M}, [a, b] \Vdash$ *(1)* $\wedge$ *(2), and let* $b_0, b_1 \ldots, b_k$ *a* *time sequence as in Definition 1. Then, if for some* $[b_i, b_j]$ *it is the case that* $\mathbf{M}, [b_i, b_j] \Vdash p \wedge MinTime(l, p)$*, then, either* $k - j < l$ *(where* $k = |D|$*), or there exists* $b_h > b_j$ *such that* $h - j \leq l$*,* $k - h \geq 1$*, and* $\mathbf{M}, [b_h, b_l] \Vdash p$ *for some* $b_s > b_h$*.*

Proof. Let $\mathbf{M}, [a, b] \Vdash (1) \wedge (2)$, and let $b_0, b_1 \ldots, b_k$ a time sequence as in Definition 1. Suppose that for some $[b_i, b_j]$ it is the case that $\mathbf{M}, [b_i, b_j] \Vdash p \wedge MinTime(i, p)$. For the sake of simplicity, suppose $k - j \geq l$. We have to show that there exists $b_h > b_j$ such that $h - j \leq l$, $k - h \geq 1$, and $\mathbf{M}, [b_h, b_l] \Vdash p$ for some $b_s > b_h$. This can be proved by contradiction: if such a b_h does not exist, then the formula $\underbrace{\langle A \rangle p \vee \langle A \rangle (t \wedge \langle A \rangle (p \vee \langle A \rangle (t \wedge \langle A \rangle \ldots))}_{l}$ cannot be satisfied. The case $k - j < i$ can be proved in a similar way. □

Similarly, we will need a shortcut to indicate that two medical events p and q begin 'almost' at the same instant; for example, when p is a drug and q is the test that must be performed shortly after the administration of p. So:

$$After(l, p) = [\overline{A}]\,\underbrace{(\langle A \rangle p \vee \langle A \rangle (t \wedge \langle A \rangle (p \vee \langle A \rangle (t \wedge \langle A \rangle p \ldots))))}_{l},$$

which, for $i \in \mathbb{N}$, makes sure that p is satisfied at some interval beginning no more than l time units after the beginning of the current interval.

Proposition 2. *Let* $\mathbf{M} = \langle \mathbb{I}(\mathbb{D}), V \rangle$ *be any model based on (a prefix of)* $\mathbb{N}$ *such that, for some interval* $[a, b]$*,* $\mathbf{M}, [a, b] \Vdash (1) \wedge (2)$*, and let* $b_0, b_1 \ldots, b_k$ *a time sequence as in Definition 1. Then, if for some* $[b_i, b_j]$ *it is the case that* $\mathbf{M}, [b_i, b_j] \Vdash p \wedge After(l, q)$*, then, either* $k - i < l$ *(where* $k = |D|$*), or there exists* $b_h > b_i$ *such that* $h - i \leq l$*,* $k - h \geq 1$*, and* $\mathbf{M}, [b_h, b_l] \Vdash q$ *for some* $b_s > b_h$*.*

Proof. As in the previous lemma. □

Table 1: General aspects. The '`admission of the patient`' is the starting point of of our model; we will use propositional letters for the atomic medical concepts, such as *ConsTest* for '`Consciousness and focus status test`'. So, we will have:

$$\bigwedge_{p \in A} ((p \vee \langle A \rangle p \vee \langle A \rangle \langle A \rangle p) \wedge [U](p \rightarrow MinTime(l(p), p))) \quad (4)$$

where $A = \{ConsTest, APTest, EcoDopTest, GlucTest, ElectBalTest\}$, and $l(p)$ is defined for each $p \in A$.

Table 2: Sedation. The first requirement can be translated assuming that the propositional letter indicating that the room is isolated is a nominal:

$$\langle A \rangle (N(Isolated) \vee \langle A \rangle N(Isolated)) \wedge MinTime(l(Isolated), Isolated). \quad (5)$$

The second requirement is a direct application of the shortcut $After(l, q)$, as follows:

$$\bigwedge_{m_l} [U](Sedation(m_l) \wedge After(l(Sedation), APTest). \quad (6)$$

Table 1. Paragraph 1: General Aspects

Original Requirement	Abstraction	Shortcuts
Special attention will be paid to the following aspects: Consciousness and focus status, Arterial pressure, Eco-doppler test results, Glucose levels, Electrolyte balance.	From the admission of the patient, the tests for Consciousness and focus status, Arterial pressure, Eco-doppler test results, Glucose levels, and Electrolyte balance will be periodically repeated; the maximum number of time unit that can pass between any two tests of the type t is $l(t) \in \mathbb{N}$.	– $MaxTime(l, p)$ – $ConsTest$ – $APTest$ – $EcoDopTest$ – $GlucTest$ – $ElectBalTest$

Similarly, the third requirement involves $After(l, q)$, as follows:

$$\bigwedge_{m_l}[U]((Sedation(m_l) \wedge After(l(Sedation), HypoTen) \rightarrow LowerSed(m_l)), \quad (7)$$

where

$$LowerSed(m_l) = [A]((\bigwedge_{m_l} \neg Sedation(m_l) \vee \bigvee_{m_{l'}<m_l} Sedation(m_{l'}))) \wedge$$
$$[A][A]((\bigwedge_{m_l} \neg Sedation(m_l) \vee \bigvee_{m_{l'}<m_l} Sedation(m_{l'}))).$$

Table 3: Basic knowledge. In general, a CPG does not include basic knowledge (KB), such as typical effects of drugs, pharmacokinetics, etc. Nevertheless, one can include (part of) the KB as follows.

Drugs of the class of $Nitroglycerin$ or $Nitroprusside$ will be formalized as $DrugNO$; in the KB the expert must add a requirement such as:

$$[U](\bigvee_{p \in B}(p \rightarrow DrugNO)), \quad (8)$$

where B is the set of (propositional letters for) drugs of the class of $Nitroglycerin$ or $Nitroprusside$, chosen by the expert. In this way, the requirement can be simply formalized as:

$$[U](\neg DrugNO). \quad (9)$$

The other requirement is similar to the one already seen in Table 1:

$$(Nimo \vee \langle A\rangle Nimo \vee \langle A\rangle\langle A\rangle Nimo) \wedge [U](Nimo \rightarrow MinTime(l(Nimo), Nimo)). \quad (10)$$

Table 2. Paragraph 2: Sedation

Original Requirement	Abstraction	New Shortcuts
The patient will be checked into an isolated room. Sedation will be the minimal necessary to maintain the patient comfortable, conscious, and with no Arterial pressure oscillations. Special attention will be paid in order not to induce Hypotension.	`No more the` $l(Isolated)$ `times unit can pass before the patient is checked into an isolated room. After any administration of the Sedation drug, no more than` $l_1(Sedation)$ `unit time can pass before the Arterial pressure test is performed. Sedation can be administered at levels` $m_1 < m_2 < \ldots$, `and, if Hypotension is detected no more than` $l_2(Sedation)$ `time units after administrating the Sedation drug at level` m_l, `then the next level` m_o `must be lower.`	– $After(i, p)$ – $Isolated$ – $Sedation(m_l)$ – $HypoTen$

Table 3. Paragraph 3/4: Nimodipine and drugs of the class of Nitroglycerin or Nitroprusside

Original Requirement	Abstraction	New Shortcuts
It is not recommended the use of drugs of the class of Nitroglycerin or Nitroprusside. All patients will be administrated with Nimodipine during all the treatment	`No drug of the class of Nitroglycerin or Nitroprusside can be administrated. After any administration of Nimodipine the maximum number of time units that can pass before the next one is` $l(Nimodipine)$.	– $DrugNO$ – $Nimo$

4 Discussion and Conclusions

In general, the classical choice of a temporal logic for practical purposes is a point-based one. The reasons can be found in the good computational properties of these kinds of logics, and in their intuitive syntax/semantics. As we have recalled, PNL constitutes an exception in the field of interval-based temporal logics, especially because it is decidable and it is powerful enough to embed the whole LTL[F,P] [3]. The decidability of the satisfiability problem can be successfully used to solve the following problem: *Is the CPG G sound?*, which corresponds to the following logical problem:*Is the formula φ_G satisfiable?*, where φ_G is the formula corresponding to the CPG G as in our case-study. The satisfiability problem for PNL has been solved over $\mathbb{N}$ by means of a sound, complete, and terminating tableau method; this means that even if the worst-case complexity is high (NEXPTIME), in practical terms it can be lowered by using any kind of optimizing techniques commonly applied in tableau methods.

Finally, we are currently approaching the *model checking* problem for PNL. This method can be used in the context of the present paper to solve the following problem: *Has the patient P been treated coherently with the CPG G?*, which corresponds to the following logical problem: *Does the model M_P satisfy the formula φ_G?*, where the model M_P is the formalization of the records for the patient P in form of a (possible) model for PNL.

In conclusion, we considered a complete case-study, namely a Spanish clinical guideline for no-traumatic subarachnoid hemorrhage, and we showed a possible translation into PNL of the time-related medical events and treatments. Then, we illustrated how it is possible to take advantage from such a formalization and from the recent advances on automatic deductive methods for PNL to prevent possible (qualitative) contradictions, both in the guideline and with the general medical knowledge.

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References

1. Allen, J.F.: Maintaining knowledge about temporal intervals. Communications of the ACM 26(11), 832–843 (1983)
2. Bresolin, D., Goranko, V., Montanari, A., Sala, P.: Tableau Systems for Logics of Subinterval Structures over Dense Orderings. In: Olivetti, N. (ed.) TABLEAUX 2007. LNCS (LNAI), vol. 4548, pp. 73–89. Springer, Heidelberg (2007)
3. Bresolin, D., Goranko, V., Montanari, A., Sciavicco, G.: On Decidability and Expressiveness of Propositional Interval Neighborhood Logics. In: Artemov, S.N., Nerode, A. (eds.) LFCS 2007. LNCS, vol. 4514, pp. 84–99. Springer, Heidelberg (2007)
4. Combi, C., Gozzi, M., Juarez, J.M., Marin, R., Oliboni, B.: Querying clinical workflows by temporal similarity. In: Bellazzi, R., Abu-Hanna, A., Hunter, J. (eds.) AIME 2007. LNCS, vol. 4594, pp. 469–478. Springer, Heidelberg (2007)
5. Dazzi, L., Fassino, C., Saracco, R., Quaglini, S., Stefanelli, M.: A patient workflow management system built on guidelines. In: Proc. of AMIA Annu. Fall Symp., pp. 146–150 (1997)
6. de Clercq, P.A., Blom, J.A., Korsten, H.H.M., Hasman, A.: Approaches for creating computer-interpretable guidelines that facilitate decision support. Artificial Intelligence in Medicine 31(1), 1–27 (2004)
7. Field, M.J., Lohr, N.K.: Guidelines for Clinical Practice: from Development to Use. National Academic Press, London (1992)

8. Fox, J., Johns, N., Lyons, C., Rahmanzadeh, A., Thomson, R., Wilson, P.: Proforma: a general technology for clinical decision support systems. Computer Methods and Programs in Biomedicine 54(2), 59–67 (1997)
9. Gabbay, D.M., Hodkinson, I.M., Reynolds, M.: Temporal Logic: Mathematical Foundations and Computational Aspects. Oxford University Press, Oxford (1994)
10. Goranko, V., Montanari, A., Sciavicco, G.: Propositional interval neighborhood temporal logics. Journal of Universal Computer Science 9(9), 1137–1167 (2003)
11. Halpern, J., Shoham, Y.: A propositional modal logic of time intervals. Journal of the ACM 38(4), 935–962 (1991)
12. Hederman, L., Smutek, D.: Representing clinical guidelines a comparative study in uml (2002)
13. Hommersom, A., Lucas, P., Balser, M.: Meta-level verification of the quality of medical guidelines using interactive theorem proving. In: Alferes, J.J., Leite, J. (eds.) JELIA 2004. LNCS (LNAI), vol. 3229, pp. 654–666. Springer, Heidelberg (2004)
14. Lucas, P.: Quality checking of medical guidelines through logical abduction. In: Proc. of the 23rd SGAI International Conference on Innovative Techniques and Applications of Artificial Intelligence (AI 2003), pp. 309–321 (2003)
15. Ohno-Machado, L., Gennari, S.: The guideline interchange format: A model for representing guidelines. Journal of the American Medical Informatics Association 5(4), 357–372 (1998)
16. Panzarasa, S., Stefanelli, M.: Workflow management systems for guideline implementation. Neurological Sciences 27(3), 245–249 (2007)
17. Sciavicco, G.: Quality checking of medical guidelines using interval temporal logics. In: Proc. of the 12th Conference CAEPIA (Conferencia de la Asociación Española para la Inteligencia Artificiál) (2007)
18. Shahar, Y., Miksch, S., Johnson, P.: The asgaard project: a task-specific framework for the application and critiquing of time-oriented clinical guidelines. Artificial Intelligence in Medicine 14(1-2), 29–51 (1998)
19. Suarez, J.I., Tarr, R.W., Selman, W.R.: Aneurysmal subarachnoid hemorrhage. New England Journal of Medicine 354, 387–396 (2006)