Representation Primitives, Process Models and Patient Data in Computer-Interpretable Clinical Practice Guidelines:

A Literature Review of Guideline Representation Models

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SUMMARY

Representation of clinical practice guidelines in a computer-interpretable format is a critical issue for guideline development, implementation and evaluation. We studied eleven types of guideline representation models that can be used to encode guidelines in computer-interpretable formats. We have consistently found in all reviewed models that primitives for representation of actions and decisions are necessary components of a guideline representation model. Patient states and execution states are important concepts that closely relate to each other. Scheduling constraints on representation primitives can be modeled as sequences, concurrences, alternatives, and loops in a guideline's application process. Nesting of guidelines provides multiple views to a guideline with different granularities. Integration of guidelines with electronic medical records can be facilitated by the introduction of a formal model for patient data. Data collection, decision, patient state, and intervention constitute four basic types of primitives in a guideline's logic flow. Decisions clarify our understanding on a patient's clinical state, while interventions lead to the change from one patient state to another.

INTRODUCTION

In recent years, clinical practice guidelines (CPGs) have been developed to reduce unjustified variations in clinical practice, with the goal to improve health care quality and to contain costs [1]. The Institute of Medicine (IOM) defined practice guidelines as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" [2]. The importance of CPGs is already widely recognized since the publication of the IOM report in 1990 [2]. However, health care organizations typically pay more attention to guideline development than to guideline implementation for routine use in clinical settings [3], evidently hoping that clinicians will simply familiarize themselves with written guidelines and then apply them appropriately during the care of patients. Development of strategies to implement CPGs has thus become a critical issue.

Studies have shown that computer-based clinical decision support systems (CDSSs), when developed to provide patient-specific assistances in decision-making and integrated with clinical workflow, can improve clinicians' compliance with CPGs and patient outcomes [4-7]. Development of CDSSs has thus been proposed as a strategy to promote the implementation of CPGs [1, 8]. However, there exist several obstacles to the implementation of computer-based guideline systems. For example, translation of CPGs into computer algorithms from their published formats, which are typically not computer interpretable, is not an easy task. In addition, integration of guideline systems with electronic medical records (EMRs) is difficult to be generalized [9]. A potential solution to these problems is the development of a common model for guideline representation [10, 11].

A formal model for guideline representation can provide in-depth understanding of the clinical care processes addressed by CPGs. For example, a guideline representation model can provide the generic knowledge required in conceptual modeling and authoring of

CPGs [11]. It can be used to identify different requirements by clinicians for assistance during the process of decision-making [12]. A common guideline representation model can support automatic verification and validation of CPGs [13, 14]. It can also be used to facilitate standard approaches to guideline dissemination [15] and local adaptation [16]. Finally, a standard guideline representation model can be used as a generic template in the integration of CPGs with the healthcare information system at a local institution [17] and assist the maintenance of the guideline system itself [18].

In this paper, we review the literature of the current research on guideline representation models. During the review, we aim to extract common representation primitives and process structures from different models. We hope these common representation primitives and process structures could improve our understanding of the requirements in the development, implementation and evaluation of computer-interpretable CPGs, and particularly their relationship to a patient's clinical status in the context of CPGs. This research is an extension of an earlier work that reviewed the literature of guideline representation models [19].

METHODS

Inclusion of guideline representation models as subjects in our review was based on the following criteria: (a) the subject models should be computer-interpretable and were intended to be integrated with EMRs to provide patient-specific assistances in clinical decision making, and (b) the subject models were developed and implemented specifically for the representation of CPGs. In other words, models developed to represent paper-based CPGs such as clinical algorithm [20] and guideline document model such as GEM [21] were not enrolled as subjects in the review. Furthermore, generic knowledge representation formalisms such as production rules, decision tables and decision trees, although could be used for guideline representation, were not considered to be relevant for the purpose of this review.

We searched MEDLINE using (a) "practice guidelines" as a subject heading, and (b) "knowledge representation" or "model" as keywords. We combined the results of (a) and (b) and performed a manual review for relevant subjects. We complemented the result by a review of papers published in *the Journal of the American Medical Informatics Association*, *International Journal of Medical Informatics, Artificial Intelligence in Medicine*, *Methods of Information in Medicine*, *Medical Decision Making*, *Medinfo, and the Proceedings of AMIA Symposium*. The references cited in the reviewed publications and our personal accumulation of literatures were also searched to pursue completeness. Inclusion of a guideline representation model in the review was based on our subjective decision based on the criteria defined above. In case there were multiple published releases for a guideline representation model, the features of these models discussed in the following sections were based on the most recent one.

Based on the criteria defined, we selected eleven guideline representation models in the review. These guideline representation models include the Arden Syntax developed at Columbia University [22], the DILEMMA/PRESTIGE model developed in Europe [23], the EON/DHARMA model developed at Stanford University [24, 25], the PROforma model developed at the Imperial Cancer Research Fund in the United Kingdom [26, 27], the guideline representation model in the Siegfried system developed at Duke University (hereafter referred to as Siegfried model) [28], the GLIF model developed by the InterMed Collaboratory [18, 29], the Asbru model originally developed at Stanford University and currently maintained by Vienna University of Technology and Ben-Gurion University [30], the GUIDE/PatMan model developed at the University of Pavia [31], the PRODIGY model developed at the University of Newcastle [32], the guideline representation model in the GASTON framework developed at the University of Maastricht (hereafter referred to as GASTON model) [33], and the guideline model developed at the University of Torino (hereafter referred to as Torino model) [34].

Dimensions of the review include (a) representation primitives that constitute the basic components of a guideline representation model, (b) structural arrangement of these representation primitives that forms the application process of CPGs, and (c) modeling of patient data. We believe that these features are part of the basic requirements to a guideline representation model for computer-based implementation of CPGs.

REPRESENTATION PRIMITIVES

All of the reviewed models contain primitives that are used to represent specific clinical tasks. These primitives, according to the type of the tasks they intend to represent, could be classified into two categories, actions and decisions. Most of the reviewed models also contain primitives that are used to represent intermediate state of a specific context during the application of CPGs. These intermediate states could be either patient states that describe the clinical status of a patient, or execution states that describe the situation of a guideline implementation system.

An *action* is a clinical or administrative task that is recommended to perform, maintain, or avoid during the process of guideline application, for example, recommendation of a medication or invocation of another guideline. A *decision* is a selection from a set of alternatives based on predefined criteria in a guideline, for example, selection of a lab test from a set of potentials. A *patient state* in the context of a guideline is a reification of a treated individual's clinical status based on the actions that have been performed and the decisions that have been made. For example, the description of a patient who has already received the first dose of the influenza vaccine and is eligible for the second dose as in the state of *eligible-for-the-second-dose-of-influenza-vaccine* is a patient state. An *execution state* is a description of a guideline implementation system based on the stage of a task, such as the action and decision defined previously, during the process of guideline execution. For example, the description of a guideline system as *ready* for execution of the task *recommend-the-second-dose-of-influenza-vaccine* when a patient has already received the first dose and is eligible for the second dose is an execution state. We elaborate on the relationship between patient state and execution state later in the Discussion section. The primitives to represent the actions, decisions, patient states and execution states in the reviewed guideline representation models are summarized in Table 1. In the following subsections, we explain the various approaches to the representation of actions, decisions, patient states and execution states in the reviewed guideline models.

[Table 1]

ACTIONS

Actions are typically used to represent specific clinical tasks. All of the reviewed models support the representation of actions. For example, Arden Syntax has an *action slot* in its Medical Logic Modules (MLMs), which is used to encode the clinical task that should be performed [22]. GLIF has an *action step*, which is used for similar purpose [18, 29]. In some models, actions are encoded as recursive tasks that could be decomposed further. For example, DILEMMA/PRESTIGE represents guidelines as a set of *protocols* that can be refined further into subprotocols [23]. A similar approach is taken by Asbru, in which *plans* are recursively decomposed until they become atomic *plans* that can be directly executed for specific clinical purposes [30].

Actions can be classified into three categories, i.e., *clinical interventions*, *data collections*, and *wait actions*. Clinical interventions are the actions that deal directly with the management and treatment of patients, such as prescriptions and operations. Data collections, on the other hand, are the actions that do not treat patients directly. Instead, they are only used to obtain the information about patients, such as observations and examinations. In specific circumstances, even if we do nothing to patients, their underlying pathophysiological status may still change over time. We categorize these actions as wait actions. PROforma distinguishes clinical interventions from data collections by using two different types of task, *actions* and *enquiries*, with the former corresponding to clinical interventions and the latter corresponding to data collections with values that could be retrieved immediately [26, 27]. Similar primitives that are used to represent data collections can be found elsewhere, such as *temporal query* in EON/DHARMA [24, 25], *get data* action in GLIF [18] and *query action* in Torino [34]. GUIDE/PatMan has a *wait* step, which is exactly a wait action as we defined [31].

Actions can also be classified according to how promptly they can be finished. For this purpose, EON/DHARMA and PRODIGY distinguish *actions* from *activities*, where the former are typically used to represent actions that could be completed immediately such as ordering of a test and the latter are used to represent actions that will last for specific periods such as administration of a medication [24, 25, 32]. GLIF, on the other hand, uses the duration constraint to differentiate actions that could be finished immediately from those that need a specific time to complete [18].

DECISIONS

Decisions are used to represent the process of medical decision-making. During a decision process, we usually need to select a specific option from a set of alternatives based on predefined criteria. According to the definition by IOM, the purpose to develop CPGs is to assist the decision-making by clinicians and patients [2]. Consequently, all of the reviewed models support the representation of decisions. For example, in Arden Syntax, decisions are encoded in the *logic slot* of a MLM [22], while in GLIF and EON/DHARMA, decisions are represented using *decision steps* [18, 24, 25]. In Asbru, decisions are not represented explicitly as an independent component. Instead, they are encoded within the *conditions* and *preferences* of a plan that define the criteria of transition from one plan state to another [30].

Most models support the representation of decisions that are based on logical criteria. Some of the reviewed models support more complex modes for decision-making, such as those based on decision analyses. GUIDE/PatMan is an example model that supports this mode of decision-making [31]. Other models move a step further to distinguish decisions that can be made automatically by guideline implementation systems from those that need manual judgment by users. For this purpose, GLIF has two types of decision step, *case step* and *choice step*, which are used separately to represent automatic decisions and user-assisted decisions [18]. Considering that there exist very different approaches to medical decision-making, extensibility of decision mode is an important feature for a guideline representation model. For example, decision analysis in GUIDE/PatMan is implemented through an extension of its decision mode by invocation of an external function [31]. More detailed discussion on representation of decisions in guideline representation models can be found elsewhere [35].

PATIENT STATES

Patient states are used to represent specific scenarios of a patient's clinical status in the context of guideline application. In general, a guideline could not address every possible clinical scenario for all patients during its application. This will usually lead to a discrepancy between what a guideline system suggests and what really should be done for a patient. Patient states are used to address this issue to record a patient's clinical status in specific context of a guideline. In most cases, they act as entrance and exit points of a guideline for application to a specific patient. For example, PRODIGY supports the representation of patient states using *patient scenarios*, which can be used to represent specific encounters when modeling guidelines for the management of chronic diseases [32]. Similar approaches can be found in other models to represent patient states, such as *scenarios* in EON/DHARMA [24, 25] and *patient state steps* in GLIF [18].

More generically, in any specific context of a guideline, a patient's clinical status at that point assumed by the guideline developer can be considered as a patient state. As a result, every time after a decision has been made or an action has been performed, we have already assumed a new belief on patient state. In this sense, the Torino model's *conclusion* can be considered as a primitive for the representation of patient state [34].

EXECUTION STATES

Execution states are used to represent the status of an executable task during the process of guideline application. Execution states can be traced back to finite state machines (FSMs) that are used to represent generic process. These execution states, along with the transitions between different state, will constitute an execution model that is used to represent enactment of CPGs. DILEMMA/PRESTIGE, PROforma, and Asbru take this approach to guideline modeling [23, 26, 27, 30].

PROCESS MODEL

Representation primitives discussed in the previous section are the basic elements in a guideline representation model. These primitives need to be organized to form a specific process model of CPG. The process model defines scheduling constraints on representation primitives and nesting of guidelines during guideline application. Scheduling constraints specify the temporal order in which representation primitives can be executed during guideline application. Nesting of guidelines define the hierarchical relationship among guidelines. The approaches taken by the reviewed guideline models to the representation of scheduling constraints and nesting of guidelines are summarized in Table 2. We discuss them in details in the following subsections.

[Table 2]

SCHEDULING CONSTRAINTS ON REPRESENTATION PRIMITIVES

Scheduling constraints on representation primitives are used to represent the temporal order of these primitives in execution. These constraints are typically defined as *sequence* or *concurrence* of the representation primitives. Primitives in a sequence should be executed one by one according to a specific schedule, which is usually defined as a partial order. Primitives in a concurrence should be executed in parallel. Representation of simple sequence is pretty straightforward, usually defined with the *next* or *after* relation that specify the scheduling order of two consecutive primitives, such as in GLIF and PROforma [18, 27]. As defined in Asbru, concurrence and sequence, including complex sequence such as those with unknown order, can be specified in two dimensions, i.e., *ordering constraints* and *continuation condition* [30]. Ordering constraints can take on the value *parallel*, *any order* or *total order*, and continuation condition can take on the value *all completed* or *some completed*. Combination of these two dimensions results in five scheduling constraints, i.e., *do all together, do some together, do all any order, do some any order,* and *do all sequentially* [30]. A similar approach taken by EON/DHARMA and then adopted by GLIF is to use *branch step* and *synchronization step* to represent complex sequence with partial scheduling order and concurrence [25, 18]. According to this approach, a branch step defines a point in a flowchart that is followed by multiple parallel paths or paths that can be traversed in any order, while a synchronization step defines a point at which the diverged paths converge back. A continuation criterion is then defined in a synchronization step using a logical expression, which makes the representation of scheduling constraints very expressive [18].

Alternatives and *loops* are two other types of scheduling constraints. Alternatives are a set of primitives whose execution depends on specific criteria. Alternatives are usually defined together with a decision primitive, in which case the alternative that should be followed depends on the result of the decision. Loops are repetitive execution of primitives. Loops can be defined for a single primitive, such as *cycles* in Asbru [30], or can be defined for a set of primitives, such as repetitions of a subguideline in GLIF [18]. Similar approaches to represent alternatives and loops can be found in other models, such as *exclusive alternatives* in DILEMMA/PRESTIGE's protocol composition [23] and *iterations* in GUIDE/PatMan's underlying Petri Net model [31].

In terms of the overall structure, most of the reviewed models, such as EON/DHARMA, Siegfried, GLIF, GUIDE/PatMan, GASTON and Torino, represent scheduling constraints as *flowchart*-like algorithms [25, 28, 29, 31, 33, 34], while PROforma represents them as *constraint satisfaction graphs* [26, 27]. DILEMMA/PRESTIGE represents constraints on protocols using *protocol compositions* and constraints on procedure states using *state transition diagrams* [23]. PRODIGY, on the other hand, models a guideline as a diagram of state transitions between patient scenarios [32]. This approach is shown to be very useful for the representation of chronic disease guidelines, which typically contain multiple patient scenarios at different encounters and thus could not be represented as linear diagrams with single entry point [32].

Arden Syntax takes a modular approach to the encoding of medical knowledge in MLMs. Each MLM encodes a single decision and potential actions. Although an MLM can invoke other MLMs, Arden itself does not model the structure of these invocations [22]. Its ability to represent complex guidelines, which usually consist of multiple decisions, actions and patient states, is thus constrained. A way around is the use of intermediate states to link related MLMs [36].

NESTING OF GUIDELINES

Nesting of guidelines enables multiple levels of abstraction in guideline representation and provides different granularities for the views to a guideline. All reviewed models except Arden Syntax and Siegfried support nesting. This is done through recursive decomposition of *protocols* in DIMEMMA/PRESTIGE [23], inclusion of *subguidelines* in EON/DHARMA, GLIF, PRODIGY and GASTON [25, 18, 32, 33], decomposition of *tasks* in GUIDE/PatMan [31], definition of *composite actions* in Torino [34], and specification of *plans* in PROforma and Asbru [26, 27, 30].

MODELING OF PATIENT DATA

In order to be applied in clinical practice, guidelines need to be integrated with EMRs and ideally, with physician order entry systems. A critical requirement to achieve this integration is a standard definition of patient data. Most of the reviewed models support some kinds of patient data modeling, as shown in Table 2. However, there is no standard approach for the definition of patient data.

A standard definition of patient data contains at least two components, i.e., a standard data encoding system and a standard patient data model. These two components will enable references to patient data in a guideline representation model, for example, specification of decision criteria, without the need to know the implementation details. At a local institution, the standard definition of patient data can then be mapped to the implementation-specific data schema and access methods of the local EMR. In recent years, several standard controlled medical terminologies, such as SNOMED [37] and READ [38] have been developed as standards to encode patient data. Unfortunately, there is little consensus currently in the medical informatics research community on a common patient data model.

In order to have access to patient data, Arden Syntax provides an interface to the definition of data in its *data slot*. However, it does not really support any modeling of patient data [22]. Patient data definition, which is enclosed within a pair of curly braces ("{}"), is left to the local site to implement and integrate. This *curly braces problem* is one of the major hindrances for the sharability of MLMs across different institutions [39]. EON/DHARMA and PRODIGY take an ontology approach to patient data modeling with a mapping between the patient data encoded within guidelines and an external EMR [40, 41], while Torino uses a common patient data schema for this purpose [34]. A similar approach is taken by GLIF that attempts to build an internal patient data model with a standard interface to external terminologies and data models [42]. Recent work on *virtual medical* *record* may provide a more promising approach to solve the curly braces problem by building a standard patient data model on the basis of HL7 Reference Information Model (RIM) and then providing mappings between the virtual medical record and an implementation system [43].

DISCUSSION

Decisions and actions are the key representation primitives that should be provided by a guideline representation model. This observation is supported by all of the reviewed models. In other words, there are two critical requirements to the modeling of CPGs: (a) a model needs to address what clinical tasks should be performed in a specific context of a guideline, and (b) a model needs to define the criteria to select appropriate options when there exists a set of potentials. This interpretation fits well with the common sense that CPGs are used as a guide to assist decisions in clinical practice.

Explicit modeling of patient states and execution states are also important in guideline representation. However, most reviewed models support only one type of these states, at least as reported in the literature. In fact, we believe the patient state and execution state are two sides of a guideline application process. At the clinical side, patient states reflect the clinical status of a patient during the process of guideline application; while at the system side, execution states reflect the situation of a guideline implementation system at a specific time. If we consider the conditions for the transition between execution states, we can see that satisfaction of these conditions is guideline-specific and usually corresponds to the patient states as we defined above. In this sense, patient state and execution state are closely related to each other. This may explain the phenomenon that most of the reviewed models with only one type of state represented is still rather expressive. However, as patient state can be affected by changes outside the control of a guideline system, patient state and execution state may diverge from one another.

Using different approaches to model the intermediate state in guideline application also reflects the philosophy of a representation model. Those models that use patient state to represent specific scenarios in guideline application emphasize more on CPGs' role in clinical decision making, while the others that use execution state focus more on the actions in CPGs that should be performed and the resulting requirements to a guideline implementation system. Some models try to balance between these two aspects in guideline modeling. For example, PROforma not only has a logical foundation that strictly defines the property of a guideline task, but also uses structures such as constraint satisfaction graph to model scheduling requirements in practice. More recently, modeling of the clinical side of a guideline application process seems to be recognized as more and more important. For example, Bury et al have found that patient scenarios are necessary in guideline modeling, and they have successfully modeled patient scenarios using the existing structures in PROforma [44]. This result also fits consistently with our previous observation that patient state and execution state are closely related to each other.

Decision-making is based on available patient data and other related information. One category of actions we previously defined, data collection, needs to be performed before a decision can be made, although in many cases this is specified only implicitly by virtue of the use of data in a decision criterion. Patient state is often used as an entry or exit point for a guideline, but theoretically it can be modeled at any place in a guideline's process flow. We thus define patient state based on decisions that have been made and actions that have been performed in the context of a guideline. With this definition, the process to make a decision is in fact a clarification or a refinement of belief on patient state. The patient state confirmed after a decision has been made but before any subsequent action has been performed can be seen as the description of a patient with an extra-level of information that is defined by the decision criteria. Finally, if we combine two other categories of actions, clinical intervention and wait action, into an *intervention* group, it can be considered as the cause of change from one patient state to another. The relationship among these representation primitives in a guideline's logic flow is shown in Figure 1.

[Figure 1]

This review has focused on guideline representation primitives, process models, and their relationship with a patient's clinical status. We do not attempt to review every aspect of a guideline representation model. Reviews on other features of a guideline representation model and implementation systems can be found else where, such as Tu et al's work on high-level guideline representation formalisms and the computational methods associated with them [45], Peleg et al's work on system and engineering features of a guideline model's representations for decisions, actions, data and knowledge [35, 46], Fox's work on the quality and safety aspects of guideline representations [47], and Shiffman's work on guideline implementation systems [48].

CONCLUSION

Primitives to represent clinical task of decisions and actions have been consistently identified as necessary components of a guideline representation model. Patient states and execution states are important concepts in guideline representation that are closely related to each other. Guideline structures can be modeled with scheduling constraints on representation primitives such as sequences, concurrences, alternatives and loops. Nesting of guidelines provides views to a guideline with multiple levels of abstraction. Modeling of patient data is critical for guideline's integration with EMRs and order entry systems. Data collection, decision, patient state, and intervention constitute four basic types of primitives in a guideline's logic flow, where a decision clarifies our knowledge on a patient's clinical state and an intervention leads to the change from one patient state to another.

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Table 1. Representation primitives for actions, decisions, patient states, and execution states in the reviewed guideline representation models.

Guideline Models	**Actions**	**Decisions**	**Patient States**	**Execution States**
Arden Syntax	action slot	logic slot	no	no
DILEMMA/PRESTIGE	protocol	state transition	n/a	procedure state
EON/DHARMA	action, activity	decision	scenario, activity state	no§
PROforma	action, enquiry	decision	n/a	task state
Siegfried	recommendation	logic	no	no
GLIF	action step	decision step	patient state step	no§
Asbru	plan	condition, preference	temporal patterns	plan state
GUIDE/PatMan	task, wait, monitor	decision	(implicit in Petri Net)	n/a
PRODIGY	action, activity	decision	scenario	n/a
GASTON	action	decision	n/a	n/a
Torino	work action, query action	decision action	conclusion	n/a

n/a: information not available from the publications
§ EON/DHARMA and GLIF has execution states, but they are not in the guideline representation model

Table 2. Scheduling constraints on representation primitives, nesting of guidelines, and modeling of patient data in the reviewed guideline representation models.

Guideline Models	**Scheduling Constraints**	**Nesting of Guidelines**	**Modeling of Patient Data**
Arden Syntax	module invocation	no	no
DILEMMA/PRESTIGE	protocol composition, state transition diagram	protocol	patient record model
EON/DHARMA	flowchart	subguideline	EMR ontology
PROforma	constraint satisfaction graph	plan	patient data definition
Siegfried	unidirectional graph	n/a	relations
GLIF	flowchart	subguideline	domain ontology
Asbru	plan-body	plan	n/a
GUIDE/PatMan	flowchart	task	relations
PRODIGY	state transition diagram	subguideline	EMR ontology
GASTON	flowchart	subguideline	domain ontology
Torino	flowchart	composite action	patient data schema

n/a: information not available from the publications

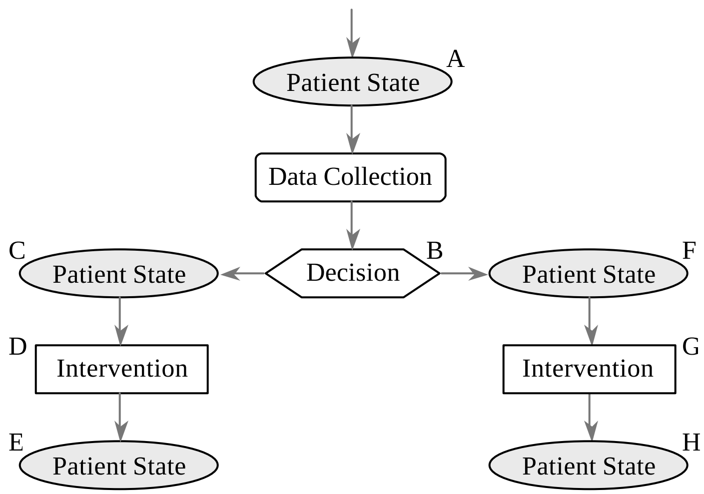

Figure 1. Guideline representation primitives in a guideline's logic flow. Here patient state C and patient state F are clarification or refinement of belief on patient state A after decision B has been made. Intervention D leads to the change from patient state C to patient state E. Similarly, intervention G leads to the changes from patient state F to patient state H.