Toward Standardization of Electronic Guidelines

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Introduction

Variation in healthcare practice that cannot be justified on the basis of differing clinical presentation has been demonstrated in the literature. [1-3] In fact, studies have shown that well accepted evidence-based guidelines exist which, if implemented, could substantially reduce inappropriate variation.[4, 5] In spite of this, guideline implementation has not progressed as would be expected. [5, 6] Numerous clinical practice guidelines (CPGs) have been produced and disseminated by a variety of government and professional organizations. Because these guidelines are largely in narrative form, they are sometimes ambiguous and generally lack the structure and internal consistency that would allow execution by computer.

The method of delivery has been shown to affect the ability of a guideline to have an impact on clinical decision-making. Guideline implementation strategies that provide patient-specific advice automatically at the point-of-care are more likely to be effective than those in which guidelines are made available in non-patient-care contexts (such as publication in monographs or journals), or where the guidelines do not incorporate patient-specific data.[5, 7] Therefore, several groups are attempting to create computer-interpretable guideline representations that can provide patient-specific decision support without interrupting clinical workflow. In addition, since the creation of computer-interpretable guidelines is time-consuming, expensive, and subject to variations, it is important to have the ability to facilitate the sharing of authoritative, well-developed guidelines among institutions and entities that wish to implement them.

Practice guidelines are defined by the Institute of Medicine as "systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances."[1] In accordance with this definition, the goals for the creation of a uniform representation of sharable electronic guidelines are fourfold. [8]

1. To facilitate reuse, as guidance may be applicable or adaptable to more than one clinical situation.
2. To support rapid dissemination of updates and changes to guidelines.
3. To make patient-specific guideline knowledge available at the appropriate point within the course of a patient's care and further to identify the appropriate components of the guideline for current clinical use in a specific case. Note that knowledge of guidelines may be available as recommendations generated by a monitoring or critiquing engine, as alerts or reminders, and not necessarily as "presentations" of guidelines to the provider.
4. To encourage guideline authors to employ rigorous techniques that will help to ensure syntactic, logical, and medical validity. By applying internal consistency checking one can decrease ambiguity, increase completeness, and decrease errors made in constructing the guideline.

In this article we describe some of the approaches to representing electronic guidelines in response to the four goals specified above, and we summarize the directions of current efforts.

Approaches to Electronic Guideline Representation

Some of the approaches to implementation of computer-interpretable electronic guidelines have been based on a formal representation specification, whereas others have been based on encoding the logic into an application-specific format not intended as a formal specification.

I. Rule-based specification

A rule-based approach for representing medical decision rules originated from research in the medical artificial intelligence community. The **HELP system** [9] is an information-management system, developed at the LDS Hospital in Salt Lake City, that has long provided decision support based on medical decision rules that can generate alerts to notify clinicians about events or conditions such as abnormal laboratory results or potentially dangerous drug interactions.

The **Arden Syntax** for Medical Logic Modules (MLMs) is a language for encoding such rules. [10] The initial version of the Arden Syntax was based largely upon the encoding scheme for generalized medical decision support in the HELP system and has been used to generate clinical alerts, diagnostic interpretations, management messages, screening for research studies and quality assurance.

The **G-CARE** language, developed at the Regenstrief Institute in Indianapolis, also utilizes rules as a means of providing decision support. It allows layers of rules to represent CPGs with tools that support complex interaction with a clinician at the point of patient care.[11]

Although the MLM or single *if-then* rule approach can be adapted to represent formal guideline knowledge that typically unfolds over time, it is not really designed for that purpose. The ability to represent such complex algorithms was demonstrated by the implementation of a care plan for the post-operative management of patients following coronary artery bypass graft surgery.[12] CPGs are typically composed of sequences of steps that have been arduously designed as a whole, instead of strings of single-step rules that are secondarily chained together.

Concurrent with much of the activity in implementation of rule-based approaches, in the early 1990's, a **frame-based** approach to representation of CPGs was developed in Germany.[13] The group who did this developed a classification-based, forward-chaining, rule-based system.

Decision tables are a related representation technique for CPGs in which rule sets are created containing recommendations that should be made given every possible combination of situations (data values) that can occur at a specific point.[14]   The method aims at verification of completeness of the rule set and enables identification of conflicting or redundant rules. Rules that contain probabilistic data of this type have also been represented as "augmented" decision tables. Decision tables, however, are not sufficiently expressive to represent most guidelines, particularly because, like rule-based representations, they do not specify the sequential nature of the decision making process that is inherent to many CPGs.

II. Decision analysis representation of guidelines

Decision analysis is a rigorous scientific approach to decision-making, which seeks to formally analyze alternatives so as to arrive at an optimal decision through the creation of decision models that incorporate probabilities for events and utilities for rating actions. These models have been used as a foundation for derivation of guidelines, by identifying thresholds and other criteria under which various alternatives become preferred. Decision analytic approaches have also been employed to augment guidelines by making use of the probabilistic data they contain for portions of guidelines where estimation is necessary. [15-18]

III. Guideline markup methods

The **Guideline Elements Model** (GEM) is a method that enables markup of the heterogeneous information contained in narrative clinical guidelines.[28] Unlike other guideline representations, GEM encodes the strength of evidence for guideline recommendations. The GEM hierarchy includes more than 100 elements. Major concepts relate to a guideline's identity, developer, purpose, intended audience, method of development, testing review plan and knowledge components.

IV. Multi-step guidelines modeled as a hierarchical set of nested guideline tasks

Several models have been developed to represent CPGs that require complex combinations of steps. All of these methods represent guideline knowledge in an object-oriented fashion.

The **Prodigy** (**P**rescribing **R**ati**O**nally with **D**ecision-support **I**n **G**eneral-practice stud**Y**) project is funded by the National Health Service of the United Kingdom. The goal of this project is to develop a guideline-based decision-support system to assist general practitioners with patient care.[19] In the Prodigy model, a guideline recommendation is considered to be appropriate for various combinations of patient states (*scenarios*) given a particular diagnosis. In turn, a scenario may have different strategies for treatment. Each of these strategies can then be further broken down into more detailed instructions. The model has been under development since 1995 and the most recent version (Prodigy 3) is commissioned to address chronic disease management, such as hypertension or diabetes. To facilitate knowledge engineering by domain experts, Prodigy aims at producing the simplest, most understandable guideline model sufficiently expressive to represent chronic disease management guidelines. It uses various techniques for managing complexity of guideline models, such as partitioning a clinical algorithm into *management algorithms* that model decisions alternatives, *consultation templates* that define context-sensitive best-practice data-collection and evaluation recommendations, and *subguidelines* that refine scenarios and decision alternatives. The Prodigy model splits clinical interventions into actions, which are instantaneous, and activities that are started and persist until they are modified or stopped.

The Prestige project, a cooperative effort at multiple European sites, represents guidelines as a structured set of subprojects. The project focuses on both guidelines and protocol-based care, as well as on resource management in the daily practice of healthcare.[20] The conceptual model and architecture grew from and extends **DILEMMA** (protocol knowledge representation), **NUCLEUS** (clinical act management) and **GALEN** (concept representation and term manipulation). These are all projects supported by the European Commission for healthcare telematics.[21]

DILEMMA began as a project within the 1991-94 AIM program of the European Commission to develop computerized decision support, particularly for prescribing drugs.[21] It is an object model that contains an activity hierarchy, with the state transitions specified for these activities. A protocol typically consists of actions and activities that need to be carried out in order to perform the appropriate clinical tasks. A protocol may also be a component of another protocol. When a protocol is implemented, a procedure, defined as a type of action, may be generated. This procedure assumes one of many action states (e.g., relevant, established, requested, accepted, cancelled). Subsets of transitions between states are pre-determined (e.g., from requested to completed). A transition is further controlled by state-transition criteria. The state-transition criteria are responsible for controlling the sequences in which protocols are implemented. Criteria are evaluated to select the protocols that are relevant at any given time. The foundations of the DILEMMA project were laid by the LEMMA project, the main objective of which was to apply a "logic engineering" approach to cancer therapy.[22] The logic-engineering approach was previously used to design and implement the Oxford System of Medicine – a decision support system for general practitioners.

PRO*forma*, is a system that has been developed at the Imperial Cancer Research Fund (UK) over the last few years for specifying clinical guidelines and protocols.[22, 23] It provides a formal mechanism for specifying the patient data, medical knowledge, tasks that represent CPGs, and the constraints among them. The basic tasks or objects supported by PRO*forma* include a plan, a decision, an action and an inquiry step. Templates are available for specifying the knowledge required for a task. A graphical knowledge editor for the creation of CPGs complements the knowledge representation model. The editor performs consistency and completeness checks prior to creating embeddable objects or steps. An enactment engine for testing and execution is also available as a stand-alone application or for use within a clinical information system.

Asbru is an intention-based language that was developed at Stanford University for the representation of CPGs.[24] Asbru permits the explicit representation of CPG intentions (i.e., goals), patient states and prescribed actions, all of which have temporal patterns. Actions (specific tasks to be performed), plans (specifications of guidelines and their individual components), and intentions (goals to be achieved, maintained or avoided at various levels of the guideline) comprise the basic concepts. A plan is composed

of a set of sub-plans. A sub-plan is referred to as an action when it can no longer be decomposed. Plans have states (started, completed, suspended, restarted, aborted). State transition criteria specify transitions between states, as described for Prestige. The plans may be sequential, parallel, or cyclical.

Finally, intentions, states and actions are expressed as temporal patterns with a time annotation and support for multiple time lines (e.g. different zero points). This enables expression of time interval-based intentions (e.g., avoid a third episode of anemia), patient states and actions.

EON[25] is a component-based representation system being developed at Stanford University. It contains knowledge structures to represent parts of a CPG. These include domain ontology, eligibility criteria, abstraction definitions, guideline algorithm, revision rules, and a temporal query language. Patient data are obtained from a database with a specified temporal database manager or from user input. Recommendations are then generated based on the specific CPG.

Recent additions to EON include the development of specialized guideline models to satisfy specific requirements of different classes of guidelines. These requirements are conceptualized in terms of a set of guideline tasks: decision-making, specification of work to be performed, interpretation of data, and setting goals. Guideline developers who use EON select modeling solutions for these guideline tasks from a toolkit. For example, for the purpose of modeling chronic disease guidelines, the EON guideline model can be specialized to one similar to that of Prodigy.[26]

The guideline algorithm is represented as a set of scenarios, action steps, decisions, branches, synchronizations, and repetition nodes that are connected by a "followed_by" relation. The decision and action steps may have goals (represented as Boolean criteria) associated with them. A *scenario*, similar to Prodigy (above), is a partial specification of a patient state. It allows the clinician to properly classify a patient into an appropriate state within a CPG. Action and activity are implemented in a manner similar to Prodigy.

EON employs three criteria languages to provide medical expressivity: (1) a simple object-oriented language; (2) a temporal query and abstraction language; and (3) first-order predicate logic. Advantages of EON include the reusability of medical domain knowledge, temporal queries and abstractions.
EON, and its application to the treatment of AIDS called T-Helper, trace their ancestry from the **ONCOCIN** project. ONCOCIN [27] was a therapy-advice system designed for use by physicians in the treatment of cancer patients. An oncology protocol is modeled as a skeletal plan consisting of a hierarchy of actions and their sequence. To represent the skeletal plan and the refinement knowledge, the system must represent the hierarchy of plan components, the sequence of plan actions, and the heuristic knowledge, represented as rules and tables, that map the patient's responses to past therapies to modifications of the standard treatment actions. Since 1998, a strong collaboration developed between EON and Prodigy projects. The EON project also contributed to, and benefited from, the GLIF development effort described below.
The **Guideline Interchange Format** (GLIF) is a model for representing guidelines.[8] The main goal is to develop a standardized approach that will facilitate sharing of computer-based CPGs. The GLIF specification consists of an object-oriented model and corresponding text syntax. It contains a set of classes that represent CPG content, each with specific data types and attributes. Collections of steps are linked together to define the flow of control of a CPG. The GLIF language is being developed through collaboration among Stanford, Harvard, McGill, and Columbia Universities, called InterMed, using a consensus-based multi-institutional process.

GLIF version 2 (GLIF2), published in 1998[8], enabled modeling of a guideline as a flowchart of structured steps, representing clinical actions and decisions. However, the attributes of structured constructs were defined as text strings that could not be parsed, and therefore such guidelines could not be used for computer-based execution that required automatic inference.

GLIF3 [29] is a developing version of GLIF, designed to support computer-based execution. GLIF3 builds upon the GLIF2 framework but augments it by introducing several new constructs and requiring a more

formal definition of decision criteria, action specifications and patient data. There are two important extensions of GLIF2 that are being implemented in GLIF3. The first is the inclusion of a superset of Arden Syntax's logic grammar as a formal expression language for specifying decision criteria and patient states. The second extension is a domain object model that will enable GLIF3 steps to refer to patient data items that are defined by a controlled terminology that includes standard medical vocabularies (e.g., the UMLS [30]) as well as standard data models for the medical concepts (e.g., HL7's Unified Service Action Model [31]). These, along with an action specification hierarchy, enable GLIF3 to have a *computable* level of specification where the logical criteria, definitions of patient data items, clinical actions, and the flow of the guideline are formally defined. Because of this formal definition of guideline components, the CPG can be validated for logical consistency and completeness.

The *computable* level may be regarded as intermediate between two other levels, an *abstract flowchart* level and an *implementation* level. In addition to the computable GLIF3 specification, GLIF3 also retains the *abstract flowchart* specification level that was supported by GLIF2. Viewing the guideline as an abstract flowchart facilitates understanding by authors and users. A third level of specification, the *implementation* level, which is to date only partly supported by GLIF3, includes non-sharable institution-specific details that enable guidelines to be incorporated into operational information systems. The representation, therefore, explicitly separates the shareable components of a guideline from institution-specific or vendor platform-specific components that are not shareable.

GLIF3 guideline representations are exchanged in Resource Description Framework (RDF) format. This format was chosen to facilitate an open process, and replaces GLIF2's proprietary ODIF format.[32] RDF, developed under the auspices of the WWW Consortium (W3C), is an infrastructure that enables the encoding, exchange and reuse of structured metadata. RDF has an explicit model for expressing object semantics (objects and attributes) using XML (eXtensible Markup Language). An RDF Schema defines the metadata definitions of GLIF3's object model. Guideline instances that conform to the RDF Schema are specified in RDF markup. The RDF instance files and the RDF GLIF Schema are easily interchanged among institutions that use GLIF as the language for representing encoded guidelines.

In order to make the GLIF3 language understood by guideline developers, who wish to use it, it is specified using Unified Modeling Language (UML) class diagrams. [33] Sharing is also facilitated by support of multiple vocabularies and medical knowledge bases.

Currently, there are two GLIF authoring tools: Protége[34], and the GEODE Authoring Tool.[35] Both of these tools help to visualize a CPG as a flow chart.

GLIF is currently a draft standard. CPGs encode using GLIF can be linked to electronic health record systems and order entry systems. GLIF can serve as a basis for melding the other electronic guideline representation approaches into a single, coherent approach that is adopted widely to facilitate sharing of guidelines. GLIF facilitates sharing in a variety of ways:
1. It is developed using a consensus-based multi-institutional process
2. InterMed intends to follow an open process, producing products (the GLIF language, documentation, encoded guidelines) which are not proprietary
3. GLIF3 will support the use of multiple vocabularies and medical knowledge bases
4. GLIF3 incorporates complementary specifications such as the Arden Syntax logic grammar and HL7's Unified Service Action Model that can perhaps ease integration of GLIF-based systems into the clinical environment

V. Other guideline modeling approaches

GEODE-CM [36] is a system that combines guidelines with structured data entry and data retrieval from a clinical database. It models guidelines as a state-transition network, where patients transition among clinical management states following transitions that are represented by logical criteria. **MBTA** [37] was an architecture for building large knowledge-based medical systems, tailored to providing clinical reminders

and practice guidelines. It did not specify a particular syntax and was designed to be a general method for managing procedural modules and data objects, not limited to specifying computer based CPGs.

Relationships among guideline modeling activities

GLIF2 was developed after analyzing EON, Arden Syntax, GEODE-CM, and MBTA. GLIF3 evolved from analysis of the further evolution of EON and Arden Syntax, and examining the constructs of the PRO*forma* and Prestige models.

Figure 1 shows the historical development of the guideline modeling methods discussed above. A comparison among six of the guideline models previously discussed is shown in Table 1.
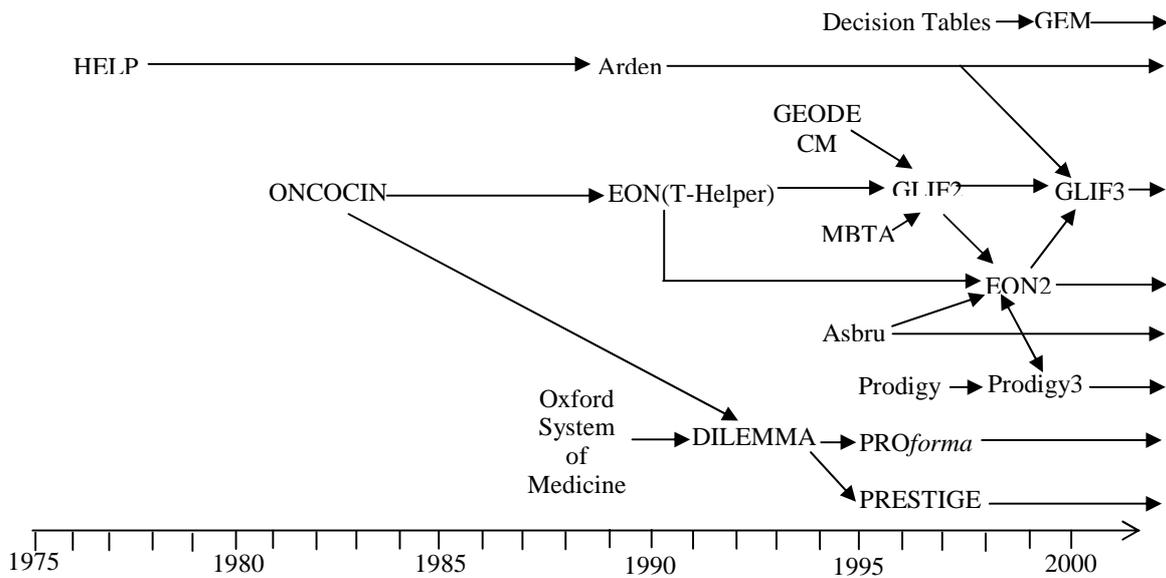
Figure 1. History of guideline modeling methods. The guideline modeling methods are positioned on a time axis according to the time at which they started being developed. An arrow between two methods originates from a method that influenced the method depicted next to the arrowhead. The diagram was prepared based on [38] and [22].

Table 1: Comparison between six guideline models

Models	GLIF	EON	Asbru	PRO*forma*	Prodigy	Prestige	GEM
Algorithmic	Yes	Yes	Yes	Not primarily	Yes	Not primarily	Not Primarily
Subguideline Support	Yes	Yes	Yes	Yes	Yes	Yes	No
Supports Decision Criteria	Yes	Yes	Yes (temporal)	Yes	Yes	Yes	Yes
Intentions and Goals Support	Possible through sub-guidelines	Yes	Yes	Yes	No	No	No
Ranking of Options Supported	Yes	Yes	No	Yes	Yes	Yes	Yes
Temporal	No	Yes	Yes	No	No	No	No

Abstractions Supported							
Explicitly Models Patient Preferences	No	No	No	No	No	No	No

Current Trends and Future Directions

The guideline community is eager to facilitate authoring of well-structured, computer-encoded guidelines that can be delivered to the point of care, and integrated into applications used by providers in the course of delivering care. While many such applications have been implemented [39] [40, 41], there has been no standardized way to represent the medical knowledge upon which such applications operate. Because of this, it is difficult to share applications and knowledge bases.

A number of organizations and research groups are engaged in developing approaches to computer-encoded guidelines for the above purposes, but there is still little standardization to facilitate sharing or to enable adaptation to local practice settings. Nonetheless, considerable progress has been made. In March, 2000, an international workshop "Toward Sharable Guideline Representation" was held in Boston, organized by the InterMed Collaboratory, and sponsored by the US Army, the Agency for Healthcare Research and Quality (AHRQ), the National Library of Medicine (NLM), and the Centers for Disease Control and Prevention (CDC). The workshop included representatives from eight different countries, among whom were stakeholders from academia, government agencies, professional organizations, insurers, providers, and industry, who recognize the need for a standard sharable computer-interpretable guideline representation format. The workshop resulted in five task forces that are pursuing a sharable guideline representation standard through exploration of functional requirements of guidelines, modeling and representation, special needs of clinical trials, infrastructure and tools, and organizational framework for continuing these activities. Any one who is interested in joining these teams is welcome to do so through the www.GLIF.org website.

The most important near-term goals are to move toward adoption of a common standard, and to create prototype authoring tools that can encode a set of medically sound, well-validated guidelines and then provide a mechanism for these guidelines to be linked seamlessly to the electronic health record.

One can easily imagine busy clinicians using information conveniently made available at the places and points in time when that information can assist them with the work-up of patients or development of management plans. It is equally easy to understand why busy clinicians in an overworked medical system fail to utilize this same information if it is accessible in a less convenient or timely fashion. Development of shareable computerized CPGs will benefit health plans that wish to reduce costs through undesirable practice variation. Most importantly, patients will benefit from reduction in adverse events and medical errors, which will result from increased integration of decision support in clinical practice.

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