AUTOMATED CLINICAL DECISION MODEL CONSTRUCTION FROM KNOWLEDGE-BASED GLIF GUIDELINE MODELS

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Summary

Clinical decision analysis is a knowledge and labor intensive task. This thesis presents a new approach to support automated construction of clinical decision models from a knowledge base. The methodology aims to facilitate application of the decision analysis paradigm in clinical domains. We make use of the knowledge-based Clinical Practice Guideline (CPG) model in Guideline Interchange Format (GLIF) as the input knowledge model. Together with the medical ontologies, which provide structured data models and controlled vocabularies for referencing patient conditions and therapies that are relevant to managing disease, it builds up the knowledge base for clinical decision making.

We develop an algorithm to automatically build a *rough decision model* (RDM) from the knowledge base described above. The RDM is a decision model that is not complete in the structure, or parameters, or both. However, it gives a neat view of the decision problem with the information extracted from the knowledge base. Rule-based references are widely used in many guideline-based decision models. We incorporate expected values computed from a decision-theoretic model to the hierarchical representation framework. In addition, it greatly reduces the efforts needed for constructing a decision model manually. With the rough model, the decision maker could construct the complete decision model by modifying the RDM and filling in additional information like probabilities and utilities.

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Chapter 1

Introduction

1.1 Background

1.1.1 Decision Analysis

1.1.1.1 Decision Problems

Decisions are any action that a problem solver may take in structuring problems in reasoning in allocating computational resources in displaying information or in controlling some physical activity [Horvitz et. al., 1988]. Many real-world decisions are hard to make due to the following reasons [Clemen 1996]:

- complexity -- many possibilities and alternatives
- uncertainty -- the future is not known for sure and available information is vague or based on estimation.
- multiple conflicting objectives -- many objectives are in conflict with each other and values of many affected parties may be different or conflicting.

- Diversity of opinions and perspectives -- different affect parties have different perspective of the problems and different people may have different risk attitude.

1.1.1.2 Decision Analysis Process

Probability provides a language for making statements about uncertainty and thus makes explicit the notion of partial belief and incomplete information. Decision theory extends probability theory, to allow us to make statements about what alternative actions are and how alternative outcomes the results of actions are valued relative to one another. Probability theory and the more encompassing decision theory provide principles for rational inference and decision making under uncertainty.

Decision analysis is an engineering discipline that addresses the pragmatics of applying decision theory to real-world problems. The Decision Analysis Process [Holtzman 1989], which consists 4 iterative phases: decision problem formulation, evaluation, appraisal and revision.

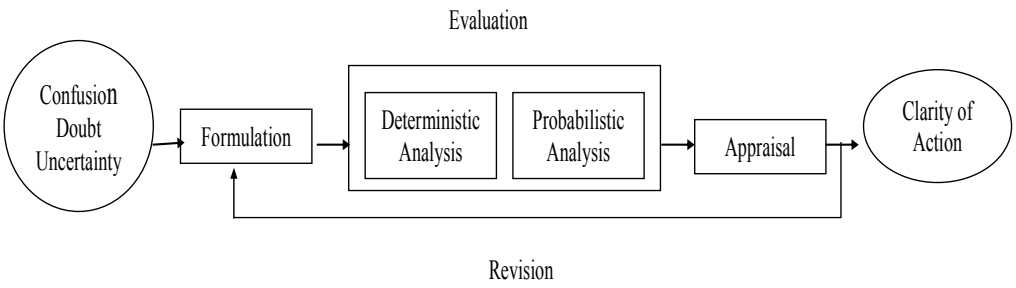

Figure 1.1 Decision Analysis Cycle

In the first phase -- formulation, the decision maker conceptualize and structure the decision problem into a model which contains the alternatives (list of possible actions that may be taken to address the problem), information (possible events and factors that are relevant to the problem), and preference or value (desirability of different consequences).

The second phase, evaluation, is to find out what is the recommended alternative. The procedure could be separated into deterministic analysis and probabilistic analysis. In the deterministic analysis, we need to construct the value model and identify the uncertainty factors that have the largest impact on the consequences. In the probabilistic analysis, probability distributions of the events and risk profile of each alternative are assessed, and then the best alternative is determined.

In the appraisal phase, more sensitivity analysis is performed to test the robustness of the recommended alternative.

The revision phase is necessary if the above three phases do not come up with a clarified action or the recommended alternative is not suitable for the problem. Then we need to restart from the formulation phase, and perform a new iteration of the decision analysis until we find the best alternative to deal with the problem.

1.1.2 Knowledge-Based Clinical Decision Making

In recent years, clinical decision analysis plays an increasingly important role in the healthcare community. Decision models (DMs) enable clinicians and analysts to assess the expected utility of alternative actions in situations that involve uncertainty, complexity, and dynamic change; to communicate explicitly assumptions about the structure of a problem; to determine the importance of uncertainty with sensitivity analyses; to determine the benefit of gathering further information through value-of-information calculation; and to make probabilistic inference conditioned on evidence [Owens and Nease 1993, Owens and Sox 1990].

Medical decision making often incorporates knowledge of the medical domain, results of published research, physicians' experiences and heuristics, patient preferences and quality of life issues. However, clinical decision analysis is a knowledge intensive task. Most of the time, the clinical model construction process is burdensome and time-consuming. Consequently, to facilitate the automation of model construction, efforts in developing knowledge-based model construction (KBMC) systems have emerged in recent years [Wellman et al. 1992, Breese et al. 1994]. It is hoped that by capturing the relevant knowledge in the knowledge bases, a well trained analyst or a domain expert would seldom be needed in the decision modeling process. Consequently, the cost of applying the decision-analytic methods in decision making could be greatly reduced [Wellman et al., 1992] [Leong, 1998].

In the medical domain, the knowledge bases usually contains ontologies, which are models describing concepts and the relationships among them, combining an

abstraction hierarchy of concepts with a semantic network of relationships. Information models (such as the Health Level 7 Reference Information Model (HL7 RIM)), and standardized vocabularies (such as Unified Medical Language System (UMLS)) can be part of an ontology. Ontology provides a core component in a knowledge-based system.

1.1.3 Clinical Practice Guidelines

The Clinical Practice Guidelines (CPGs) are defined by the Institute of Medicine (IOM) as "statements to assist practitioner and patient decisions about appropriate health care for specific circumstances" [IOM 1992]. CPGs provide a systematic means to review patient management and a formal description of appropriate levels of care, to reduce inappropriate variations in practice, to improve health care quality, and to help control costs [IOM 1992]. CPGs are being used for many different applications including screening, risk assessment, diagnosis, treatment, and monitoring of patients for a variety of medical problems.

CPGs can be represented in several different formats, including text, protocol charts or lists, flowcharts, or any combination thereof, and computer-based formats, such as The *Arden Syntax*, [Hripcsak et al., 1994], and GuideLine Interchange Format (*GLIF*) [Ohno-Machado et al., 1998] [IOM, 1992].

Some CPGs are developed based on expert opinion, local practice, or consensus. Some CPGs -- Evidence-based CPGs -- are created using well assessed, formalized medicine

knowledge and clinical literature [Evidence-Based Medicine Working Group 1992]. With the knowledge acquisition and editing tools, computerized evidence-based CPGs could be formulated as clinical knowledge models. And along with controlled vocabulary for referencing patient conditions and therapies relevant to managing disease, knowledge-based CPG models are desirable knowledge base for clinical decision making.

1.1.4 GLIF

GuideLine Interchange Format (GLIF) is a format for encoding and sharing computer-interpretable clinical guidelines developed by the InterMed Collaboratory, a joint project of medical informatics groups at Harvard, Stanford, and Columbia universities. The latest version is GLIF3.5.

GLIF will allow sharing of computer-interpretable clinical guidelines across different medical institutions and system platforms, facilitating the contextual adaptation of a guideline to the local setting and integrating them with the electronic medical record systems. GLIF has a formal representation. It defines an ontology for representing guidelines, as well as a medical ontology for representing medical data and concepts. The medical ontology is designed to facilitate the mappings from the GLIF representation to different electronic patient record systems.

1.1.5 Knowledge Acquisition and Protégé – 2000

Electronic knowledge representation is becoming more and more pervasive both in the form of formal ontologies and less formal reference vocabularies. In addition, internet has opened up an unprecedented opportunity to build up powerful large-scale medical knowledge base. In these systems, a cost-effective medical knowledge acquisition and management scheme is highly desirable to handle the large quantities of, often conflicting, medical information collected from medical experts in different medical domains and from different regions.

Protégé is an ontology-development and knowledge-acquisition environment developed by the Stanford Medical Informatics group (http://protege.stanford.edu). The current version, Protégé-2000, can run on a variety of platforms, support customized user-interface extensions, incorporates the Open Knowledge Base Connectivity (OKBC) knowledge model, interacts with standard storage formats such as relational databases, Extensible Markup Language (XML), and Resource Description Framework (RDF), and has been used by hundreds of individuals and research groups. Protégé is open source and currently has more than 7,500 registered users.

1.2 Motivations & Objectives

Clinical decision analysis is a knowledge and labor intensive task. With the knowledge acquisition and editing tools, such as Protégé-2000, computerized evidence-based CPGs could be formulated as clinical knowledge models. Along with medical ontologies, which provide a data model and a controlled vocabulary for referencing patient conditions and therapies relevant to managing disease, CPG models are desirable knowledge base for clinical decision making. We develop an algorithm to automatically generate a rough decision model, from the knowledge-based CPG model. Thus, the efforts needed for constructing a clinical decision model manually would be greatly reduced and the decision maker could construct the complete decision model by modifying the rough decision model and filling in additional information. The use of controlled vocabulary and structured data models to develop the clinical decision model will also ease the reuse and exchange of decision models among different groups of users.

In addition, many guideline-based decision models use rule-based criteria (e.g., *if* a patient is febrile and neutropenic, *then* institute broad-spectrum antibiotics) as a way of setting qualitative preferences. However, it does not incorporate uncertainty and the value of outcomes into clinical decision making. Formalizing the decision-making process forces clinicians to confront the assumptions and uncertainties underlying decisions. We envision incorporating another method: use of expected values computed from a decision-theoretic model. We will use influence diagram (which will be introduced in detail in Chapter 2) as the decision model. The proposed system architecture are shown in Figure 1.2.

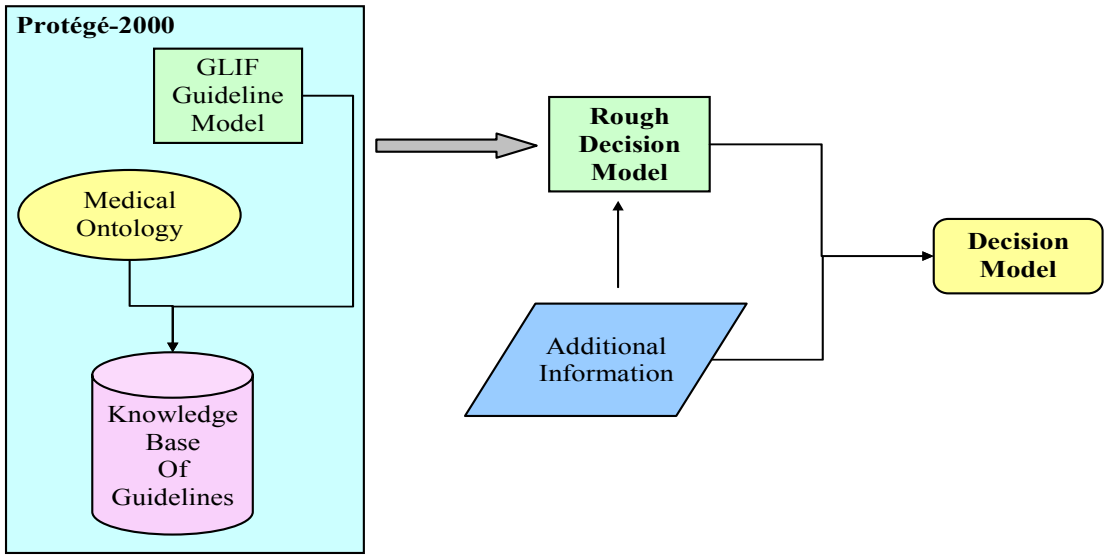

Figure 1.2 The Proposed System Architecture

1.3 Overview of the Thesis

This introductory chapter has briefly described the research background, motivations and objectives, the proposed approach and its possible application domains. The remainder of the thesis is structured as follows: Chapter 2 details the clinical decision model construction, representation and ontological features of the decision model. The knowledge-based CPG system is discussed in Chapter 3. We will introduce the Protégé knowledge model, medical ontology, and guideline model in GLIF. Chapter 4 gives a detailed description of our new methodology and system architecture, including the related works, assumptions, and the mapping from the knowledge-based GLIF guideline model to rough decision model. Chapter 5 presents a case study on applying

the proposed framework to the chronic cough management guideline model. Finally, Chapter 6 summarizes this work and discusses the contributions and limitations of our methodology, and future work.

Chapter 2

Clinical Decision Model Construction

2.1 Introduction to Clinical Decision Model

A DM, which is an abstract representation of a decision problem, takes into account the uncertain, dynamic, and complex consequences of a decision, and assigns values to those consequences [Owens and Nease 1993, Owens and Sox 1990]. In the clinical domain, a DM is a simplification of the real clinical situation; therefore, the DM reflects the decision maker's conception of how a treatment or screening intervention is used and the way in which that intervention affects the natural course of the disease, and the health status of the target patient population [Gold et al., 1996].

Guided by the characterized background information, a decision problem is formulated within the clinical context by identifying 1) the most relevant diseases/hypotheses involved, 2) the most relevant actions available, 3) the relative significance, possible outcomes, and complications of the concepts derived from 1) and 2), and their effects on each other, and 4) the evaluation criteria concerned [Owens 1997].

2.2 Decision Model Representations

In this section, we introduce some background about DM representation. Uncertainty is an inherent issue in nearly all medical problems. The prevailing method to manage various forms of uncertainty today is formalized within a probabilistic framework. Decision Trees (DTs), Influence Diagrams (IDs), Bayesian Networks (BNs), and Qualitative Probabilistic Networks (QPN) are the most common graphical representations. Among them, BN and QPNs are variants of the IDs. So we will introduce IDs in more detail.

2.2.1 Decision Trees

Traditionally decision analysis is carried out by using decision trees [Raiffa 1968]. Decision trees represent the probabilistic relationships and influences among variables in a DM according to the variables' observation ordering. An example is shown in Figure 2.1. It displays the decision tree representation for a chronic cough treatment decision problem [Lin et al, 2001], the different treatment alternatives and the corresponding treatment outcomes, and the utilities. Squares represent decisions to be made, while circles represent chance events. The branches emanating from a square correspond to the choices available to the decision maker, and the branches from a circle represent the possible outcomes of a chance event. The third decision element, the consequence, is specified at the ends of the branches. "Treat all 3" means treat all the three causes for chronic cough -- Post Nasal Drip Syndrome (PNDS), asthma, Gastroesophageal Reflux Disease (GERD) -- all together. The option do no treat all 3 are not shown in the decision tree.

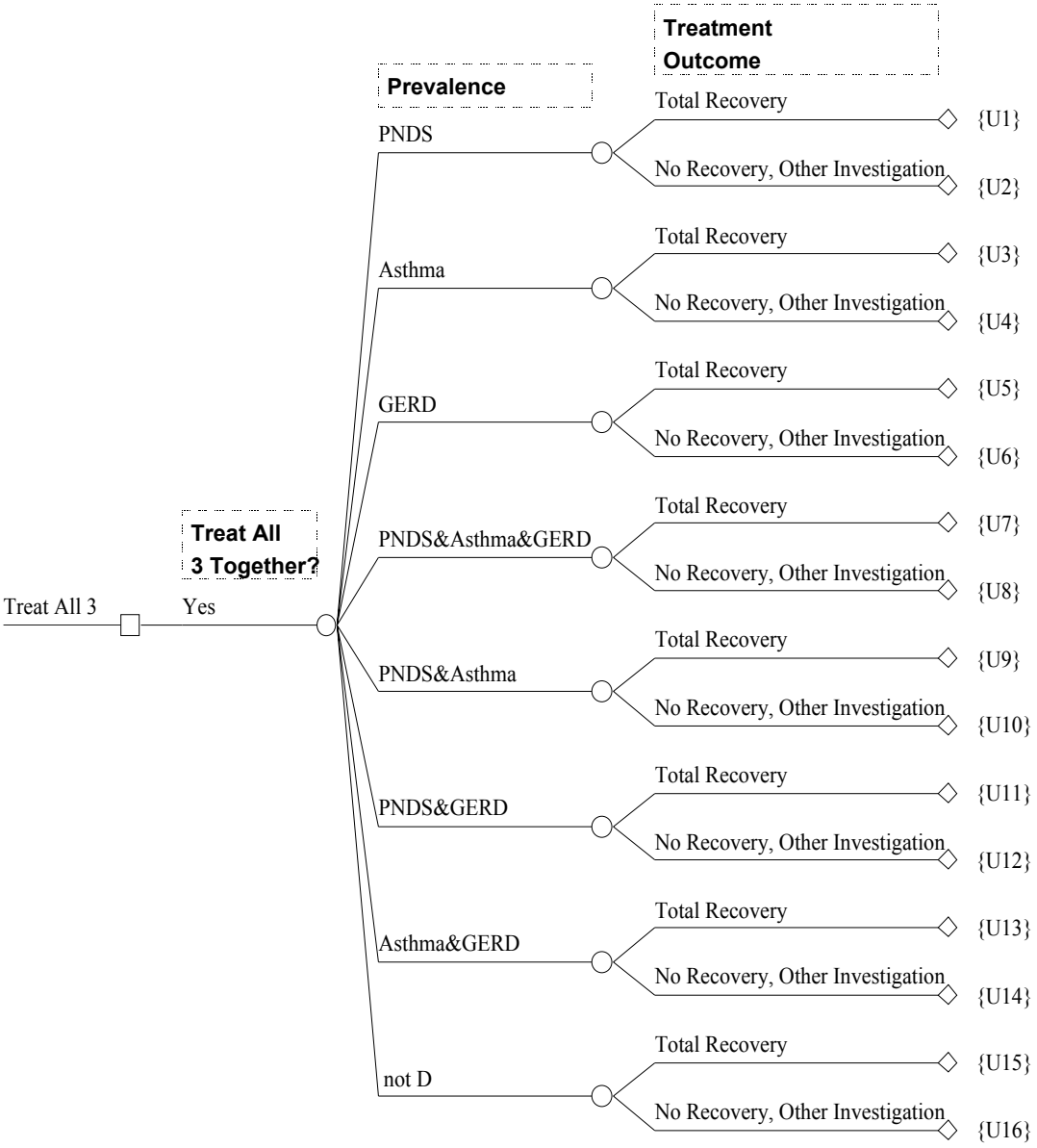

Figure 2.1 Decision Tree representation of the chronic cough treatment problem

2.2.2 Influence Diagrams

One big problem with the decision tree representation is that it grows exponentially in size as the number of relevant variables increases. A more compact framework called influence diagrams was introduced by Howard and Matheson in 1984. IDs are also

more intuitive and reveal more problem structures. They have enabled researchers to solve large decision problems that are beyond the capabilities of decision trees.

2.2.2.1 Nodes

An influence diagram is a directed acyclic graph with no cycles. There are four types of nodes. A decision node (drawn as a square), provides the decision alternatives under consideration. A chance node (drawn as a circle), represents a variable whose value is a probabilistic function. The value node (drawn as a diamond) represents the outcome of interest. Generally, each influence diagram has only one value node. Deterministic node (drawn as double oval) is a special type of chance nodes. It represents a variable whose outcome is deterministic, once the outcome on one or more of other nodes are known (e.g., cost of diagnosis and treatment).

2.2.2.2 Arcs

The directed arcs in an influence diagram represent relations between the nodes connected.

- **Relevance arc**

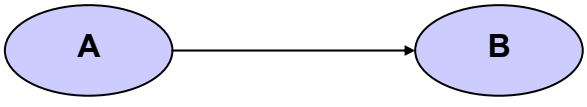

Figure 2.2 Relevance arc

The outcome of event A is relevant for assessing the chances associated with event B.

- **Influence arc**

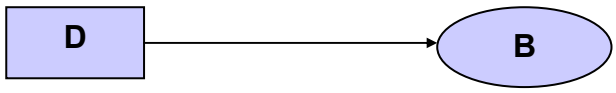

Figure 2.3 Influence arc

Decision D is relevant for assessing the chances associated with event B.

- **Information arc**

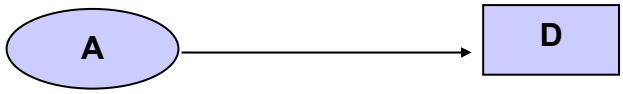

Figure 2.4 Information arc

The decision maker knows the outcome of event A when carrying out decision D.

- **Chronological arc**

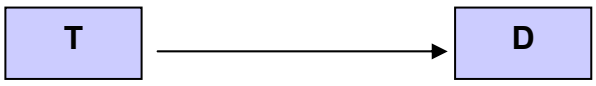

Figure 2.5 Chronological arc

Decision T is made before decision D.

- **Value arc**

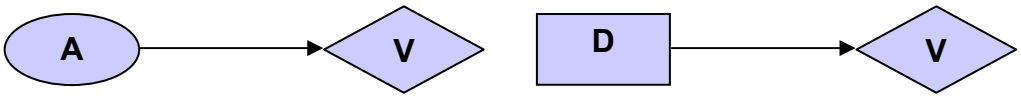

Figure 2.6 Value arc

Variable A has direct impact on Value V.

Decision D has direct impact on Value V.

Figure 2.7 shows the influence diagram for the same problem described in Figure 2.1. We could see it is a compact graphical representation of the probabilistic relationships and influences among variables in a decision model.

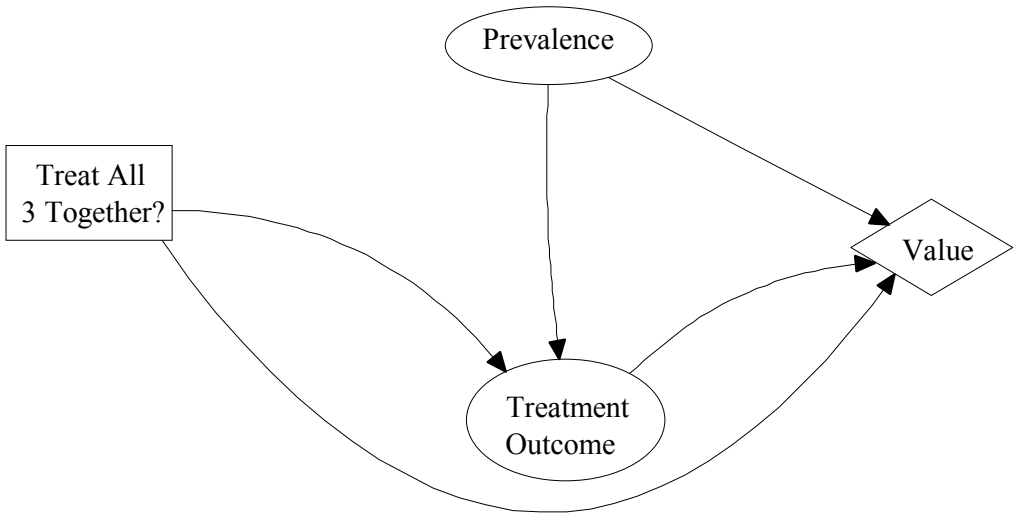

Figure 2.7 ID representation of the chronic cough treatment problem

2.2.2.3 Evaluation

Most IDs could be rolled back to decision trees. Rollback is conducted from right to left, taking expected values at every uncertainty node and selecting the best action alternative at every decision node. The ultimate purpose of building an influence diagram for a decision problem is to compute the optimal course of actions to be taken. Such a process of finding the optimal solution is called evaluating the diagram. There are two ways to solve it: 1) Convert the ID into an equivalent decision tree and use the tree roll back technique to find the solution. 2) Manipulate the ID directly by graphical operations on the nodes and arcs.

Shachter (1986) developed a method for evaluating IDs directly by arc reversal and node reduction from the ID through a series of value-reserving transformations. Each transformation leaves the expected utility unaltered, and during the operation of the algorithm the optimal decisions are computed. Shenoy (1992) described a more efficient algorithm that works on a structure similar to the ID, called a *valuation based system*. Here the nodes are removed from the network by fusing the valuations bearing on the nodes that are to be removed. Jensen et al. (1994) provided an algorithm that works on a higher-level graphical structure, the *strong junction tree*. They showed how to compile the ID into a strong junction tree, and their algorithm can be regarded as proceeding by the propagation of flows from the leaves to the strong root of the strong junction tree. During this 'collection-phase', the optimal strategy is computed. Dechter (1996) proposed a unifying framework for probabilistic inference in Bayesian networks and ID, called *bucket elimination*. It emphasizes the principle common to many of the algorithms appearing in the literature and clarifies their relationship to

nonserial dynamic programming algorithms. A general way of combining conditioning and elimination was also presented in his framework.

Besides the direct evaluation methods described above, there are some studies [Cooper 1988; Shacter and Peot 1994; Zhang 1998; Xiang et al, 2001] on reducing ID evaluation into Bayesian network (BN) inference problems that are easy to solve.

2.2.3 Bayesian Networks

IDs without decision and value nodes are called Bayesian networks (also known as Bayesian belief networks, causal networks, or probabilistic networks) [Pearl 1988]. They are widely used by Artificial Intelligence (AI) researchers as a knowledge representation framework for reasoning under uncertainty. BNs are also directed acyclic graphs with nodes representing random variables and edges representing conditional dependencies. The random variable could be either discrete or continuous. Figure 2.8 represents the well-known Asia problem which models a diagnosis problem in clinical domain.

There is a rich collection of exact and approximate algorithms for inference in BNs [Kim and Pearl 1983, Lauritzen and Spiegelhalter 1988, Jensen et al 1990, Shafer and Shenoy 1990].

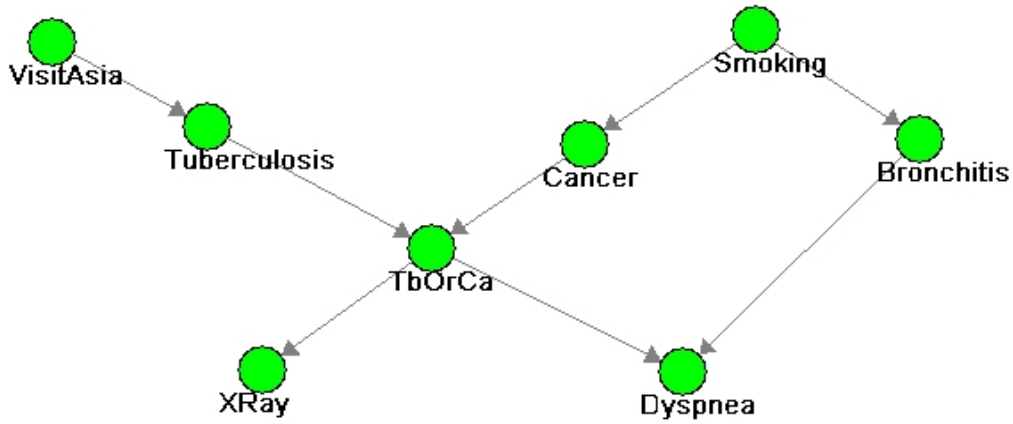

Figure 2.8 Bayesian Network representation example

2.3 Ontological Features of Clinical DM

We should not only concentrate on the structural components of the model such as nodes, conditional probabilities, and influences, but also focus on the ontological features of the decision problem such as contexts, classes of observed events, classes of available actions, classes of possible outcomes, temporal precedence, and probabilistic and contextual dependencies [Leong 1990].

To gain insights into the nature of a clinical decision, we introduce some relevant clinical concepts through a cancer treatment example. Figure 2.10 shows the nodes and their relationship of a typical disease treatment problem.

Disease & background (Chance node) Cancer affects the entire world's population, with about a threefold difference between areas with the highest and lowest age-

adjusted rates. For certain cancers, the geographic patterns are very obvious and noteworthy. In addition, some risk factors also have been identified for specific cancers, such as tobacco, alcohol, occupational hazards, environmental pollution, medicinal agents, radiation, diet and nutrition, infectious agents and genetic susceptibility. The geographic patterns and risk factors could be a set of sub-classes that represent the variables that give the background information of the disease in the class *Disease & background*. The possible outcomes of a specific chance node could be absence or presence of the factor. In addition, age, gender, tobacco, alcohol, diet and nutrition are attributes of the patient class. The graphical depiction of interconnection model of disease and background are shown in Figure 2.9.

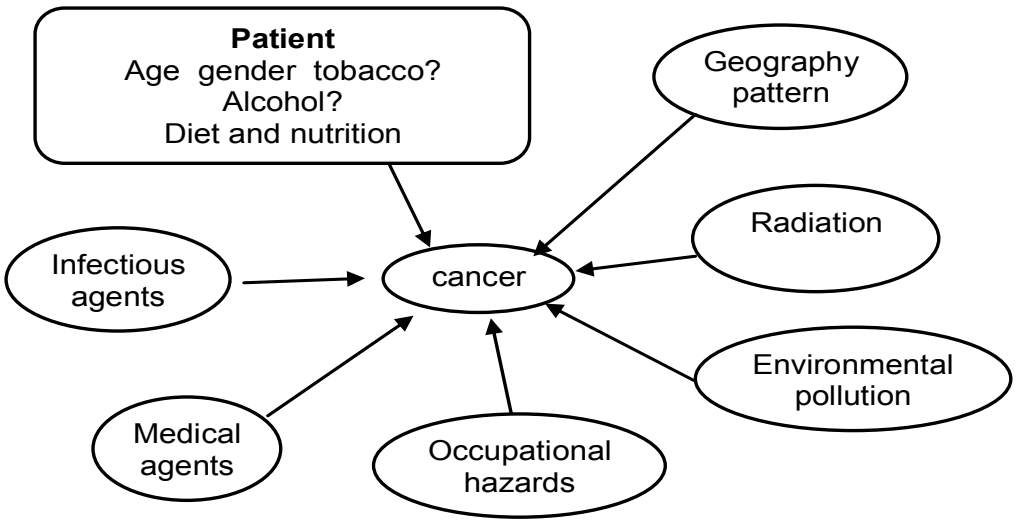

Figure 2.9 Graphical depiction of interconnection model for disease & background

Signs and Symptoms (Chance node) These are conditions observed by the physician or reported by the patient. In the graphic representation, they usually comprise a set of

classes to describe the characteristics of the disease, for example (cancer), usual behavior, rate of growth, mode of spread, local or systemic.

Test (Decision node) A diagnostic test is an action in which the existence status of a state or a process is revealed by observing the test results. The alternatives could be physical examination, laboratory tests, imaging, and biopsy. We usually associate the following properties with a test: *sensitivity*, which is a measure of how accurate the test is to confirm an infection or a disease; *specificity,* which is a measure of how accurate the test is to rule out a disease; *complications*; *mortality rate*, which is a measure of how often death results from performing the test; and *monetary costs*.

Test Result (Chance node) It is the laboratory findings of a specific test. The outcome could be only one node to state the absence or presence of the finding, positive or negative of the test. It could also be composed of a set of nodes. For example, the observation of the Mammogram in breast cancer diagnosis, is a set of nodes that include the mass findings (margins, shape, size, density, etc), associated findings (skin lesion, skin thickening, skin retraction, etc), and special cases (tubular density, lymph node, asymmetric breast tissue, etc).

Treatment (Decision node) A treatment for disease alleviates the severity of the disease. It is a set of available alternatives for treatment. The common alternatives could be chemotherapy, radiotherapy, biologic therapy, and surgery.

Treatment outcome (Chance node) It represents the possible outcomes of the treatment, like cured, improved, not-improved, worsened, death. In the oncology domain, the

possible outcomes of the treatment would include well, recurrence, metastases, recurrence and metastases.

Treatment complication (Chance node) It represents the possible complications resulting from the treatment.

Follow-up (Decision node) The follow-up process is the maintenance of contact with or reexamination of the patient, especially the following-treatment.

Follow-up outcome (Chance node) It represents the possible outcomes of the follow-up process. It could also be well, recurrent, metastatic, recurrent and metastatic, etc.

Follow-up complication (Chance node) It represents the possible complications resulting from the follow-up.

Cost (Deterministic node) It presents the amount of the monetary cost and is deterministic once the outcome of all the other nodes linked to it are known.

Quality adjusted life expectancy (*QALE*) (Deterministic node) It is a measure of the time remaining in a patient's life, taking into account the inconveniences caused by the illness (morbidity). If the outcomes of all the other nodes linked to it are known, the outcome of QALE is deterministic.

Value (Value node) It represents the overall preference conditioned on the factors affect the decision maker.

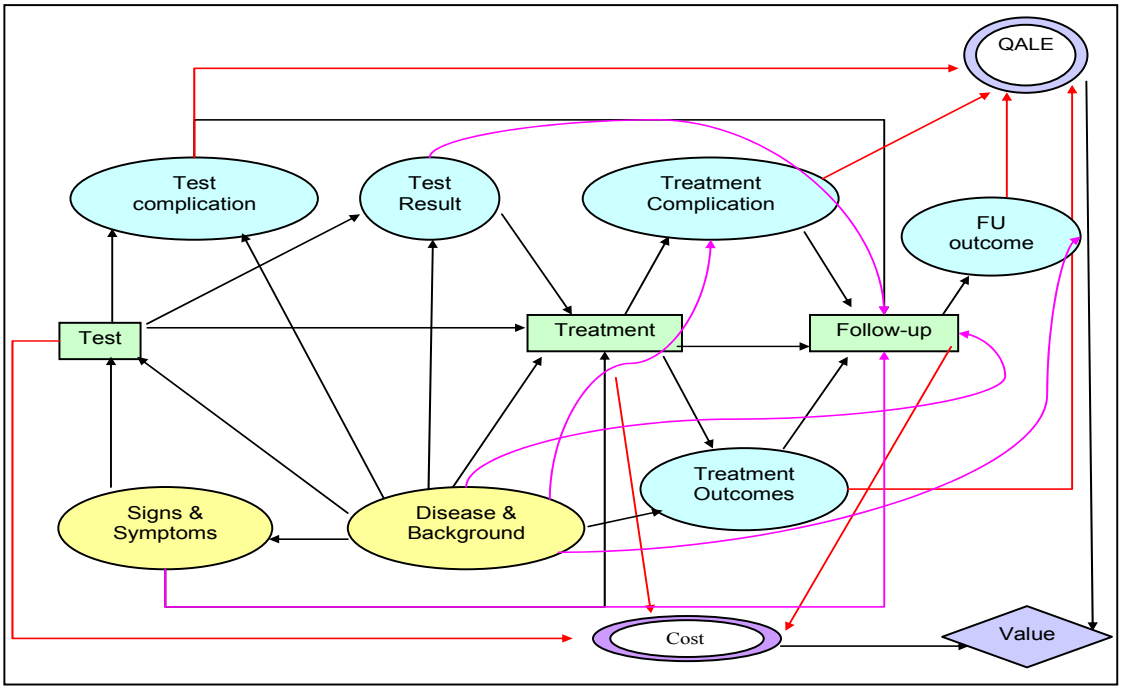

Figure 2.10 Representation of a typical clinical DM

Chapter 3

The Knowledge-based CPG system

In this chapter, we will first introduce the Protégé-2000 knowledge acquisition and editing tools. Then we will discuss the building blocks of the knowledge base, medical ontology, which is represented in 3 levels of abstraction in GLIF. The details of the GLIF guideline model are also illustrated.

3.1 Knowledge Modeling Environment – Protégé-2000

3.1.1 Introduction to Protégé

Several guideline modeling groups (e.g., EON [Musen et al., 2000], PRODIGY [Johnson et al., 2000], GLIF [Peleg et al., 2000]) and developers of decision support systems have chosen Protégé as their knowledge acquisition tool. Its automatic user-interface generation facility shows the new guideline model to the domain-specialists immediately.

Protege-2000 is an ontology-development and knowledge-acquisition environment developed by the Stanford Medical Informatics group. The current version, Protégé-2000, can be run on a variety of platforms, supports customized user-interface extensions, incorporates the Open Knowledge Base Connectivity (OKBC) knowledge model, interacts with standard storage formats such as relational databases, XML, and RDF, and has been used by hundreds of individuals and research groups. Protégé is open source and currently has more than 7,500 registered users [Gennari et al., 2002].

Protégé could also store both domain knowledge (controlled-vocabulary concepts) and large amounts of data (results from experimental studies), which are two important components for medical decision making.

3.1.2 Protégé-2000 knowledge model

Protégé uses a frame-based, hierarchical knowledge-representation system. Protégé **ontology** consists of classes, slots, facets, and axioms. **Classes** are concepts in the domain of discourse, organized in a hierarchy, and each class has at least one parent. Classes have slots whose values may or may not be inherited. **Slots** describe properties or attributes of classes. **Facets** describe properties and the data type of the slot value (e.g., string, integer, enumerated symbols, or instance of another class). **Axioms** specify additional constraints. A Protégé-2000 **knowledge base** includes the ontology and individual **instances** of classes with specific values for slots [Noy et al., 2000].

The medical knowledge base contains the domain knowledge required to formulate the decision model.

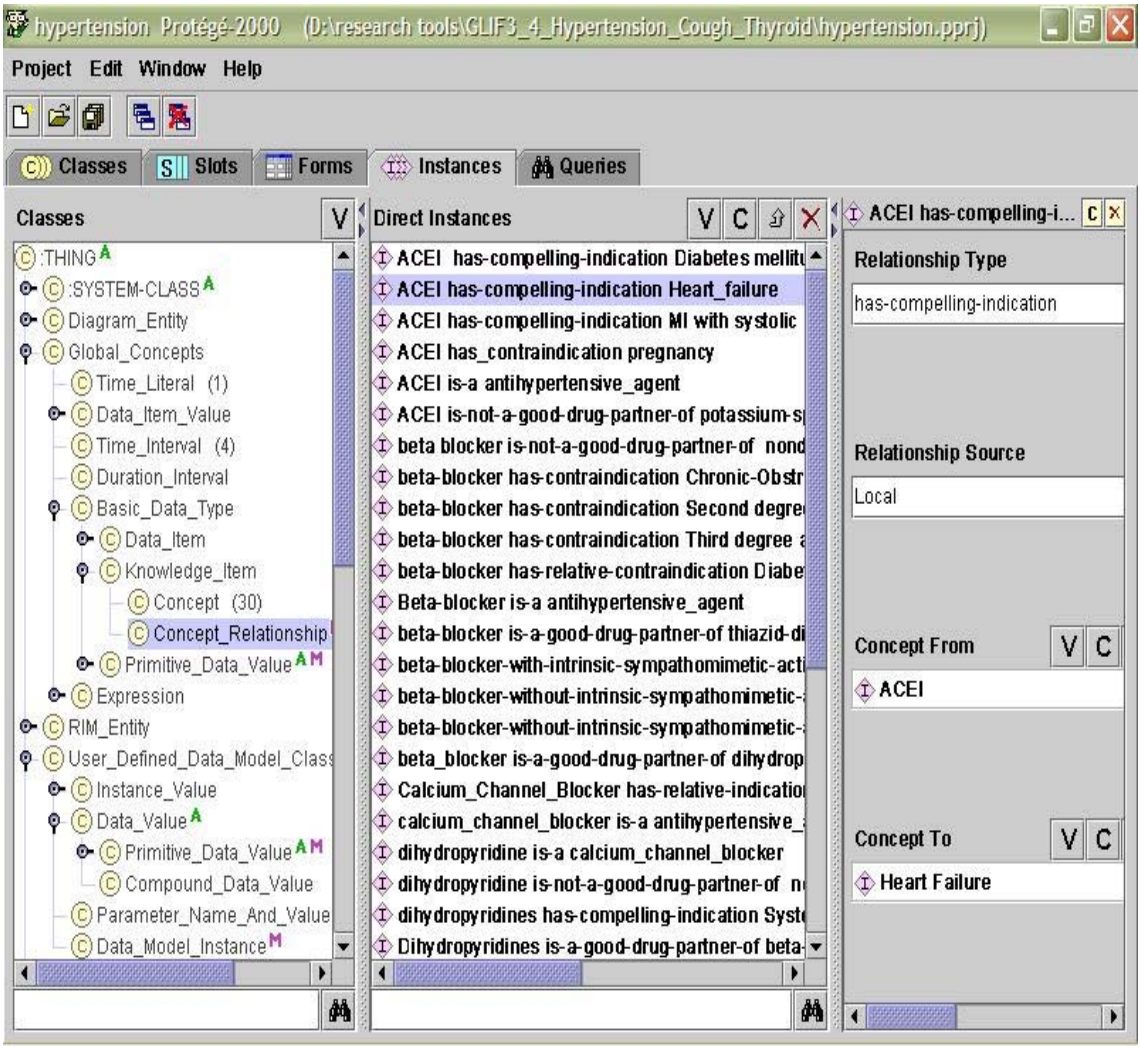

Figure 3.1 A concept hierarchy in Protégé editing environment.

3.2 Medical ontology

3.2.1 Introduction to ontology

An **ontology** is an explicit specification of the conceptualization of a domain and it provides a core component in a knowledge-based system. Information models (such as the HL7 RIM) and standardized vocabularies (such as UMLS) can be part of an ontology.

In the clinical research field, ontologies have been used in computerized guideline modeling. This allows the development of applications to provide recommendations (e.g. to make indications for the use of surgical procedures), to identify deviations in practices, and screening services (e.g. evaluate patient eligibility).

Benefits of using ontologies include: 1) Facilitating sharing between systems and reuse of knowledge; 2) Aiding new knowledge acquisition; 3) Improving the verification and validation of knowledge-based systems.

3.2.2 Medical Ontology in GLIF

The support of the ontological needs for guideline modeling in GLIF is separated into three layers, correlated to levels of abstraction. The first layer, **Core GLIF**, is part of

the GLIF specification language. It defines a standard interface to medical data items and concepts, and to the relationships among them.

The second layer, **Reference Information Model (RIM)**, is essential for guideline execution and data sharing among different applications and different institutions. It defines the basic data model for representing medical information needed in specifying protocols and guidelines. It includes high-level classification concepts, such as medications and observations about a patient, and attributes, such as units of a measurement and dosage for a drug, that medical concepts and medical data may have. The default Reference Information Model (RIM) that GLIF3 supports is HL-7's RIM version 1, also known as the Unified Service Action Model (USAM).

GLIF clinical decisions and actions refer to patient data items. Each patient **Data_Item** is defined by a medical concept, taken from some standard controlled vocabulary, and by a data model class and source. The data model class and source indicate the Reference Information Model (RIM) class and RIM model that is used for defining the data item's data structure.

The third layer, **Medical Knowledge Layer** is still under development. It will be specified in terms of the methods that it should have for interfacing to the following medical knowledge sources:

- Controlled vocabularies, like UMLS, that define medical concepts by giving them textual definitions and unique identifiers.
- Medical knowledge bases that define medical knowledge, such as drug hierarchies, and normal ranges for test results.

- Clinical repositories (EMRs)
- Other clinical applications, such as order entry systems, alert/reminder systems.

When all three layers are involved, they work closely together: Core GLIF relies on the RIM to supply the attributes of the medical concepts and to represent data values. Core GLIF relies on the Medical Knowledge Layer for accessing specific medical concepts.

In the three-layered medical ontology, users have the freedom to choose a particular RIM and a particular medical knowledge layer that fits their needs. Using a single RIM and a single controlled vocabulary to encode one guideline will ease the process of sharing the guideline, since mapping terms that belong to different RIMs and vocabularies is a difficult task. Figure 3.2 shows an example of the step hierarchy and medical ontology.

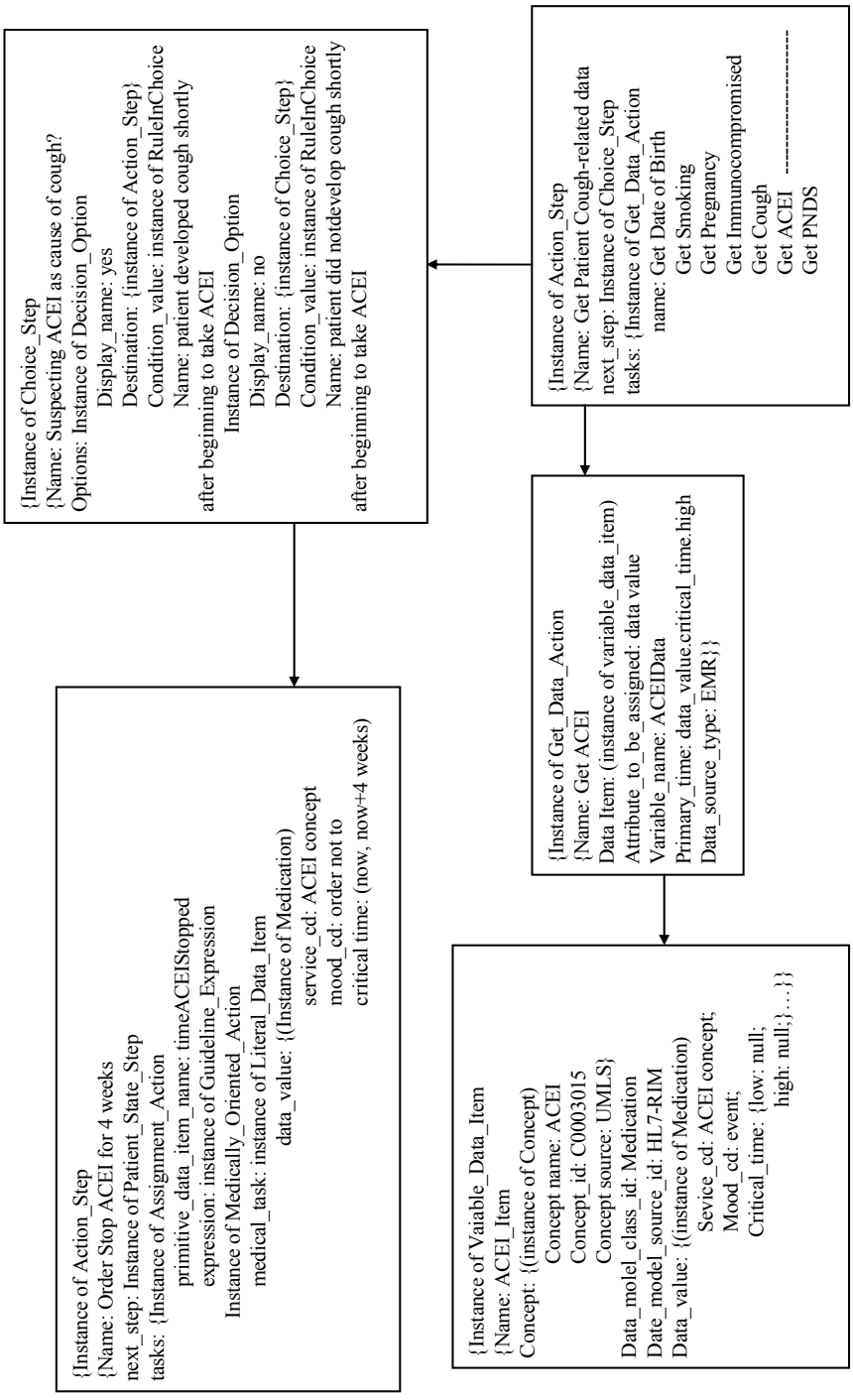

Figure 3.2 Example of the step hierarchy and medical ontology support

3.3 Clinical Practice Guideline Model in GLIF

GuideLine Interchange Format (GLIF) is a formal representation model for guidelines, created by the InterMed Collaboratory as a proposed basis for a shared representation for CPGs. InterMed is a joint project of medical informatics groups at Harvard, Columbia, and Stanford Universities, along with other participants, which has been working on GLIF since 1996. A specification for GLIF version 2.0 (GLIF2) was published in 1998 [Ohno-Machado et al., 1998]. Prototype tools for authoring, navigating, server support and execution have been developed. GLIF3 is an evolving version of GLIF, intended to address implementation more completely (see www.glif.org).

Guidelines are modeled in GLIF at three levels of abstraction. First, medical experts define a conceptual flowchart of clinical actions, decision, and patient states. Then, informaticians specify a computable specification that can be verified for logical consistency and completeness. Third, an implementable specification is created that can be incorporated into particular institutional information systems.

The GLIF3 model is object-oriented. It consists of classes, their attributes, and the relationships among the classes, which are necessary to model clinical guidelines. The model is described using Unified Modeling Language (UML) class diagrams. Additional constraints on represented concepts are being specified in the Object Constraint Language (OCL), a part of the UML standard.

3.3.1 Flowchart of GLIF

- In GLIF, guidelines are represented as a flowchart of temporally sequenced nodes called guideline steps. Different classes of guideline steps are used for modeling different constructs. The flowchart, an instance of the Algorithm class in GLIF, contains instances from 5 classes of guideline steps: Decision (case and choice), action, branch, synchronization, and patient state [Peleg et al., 2000].

- The *first_step* attribute indicates the starting point of the algorithm.

- *Next step*, *branches*, and *options* attributes of the algorithm's guideline steps provide the flow among the steps of the algorithm.

A top-level view of the GLIF model is shown in Figure 1.

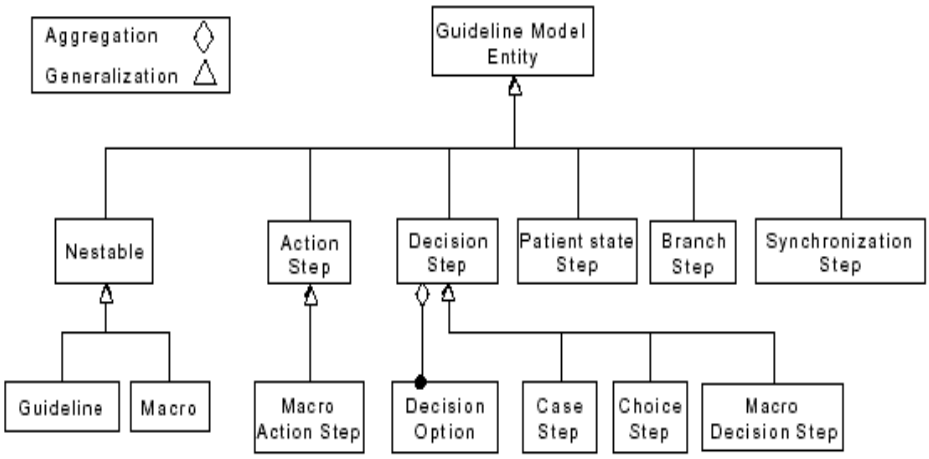

Figure 3.3 The GLIF Model, a top-level view of main GLIF classes

3.3.2 Five categories of steps

Now we will discuss in detail about the 5 categories of steps.

- **Decision_Step**

  The Decision_Step class represents decision points in the guideline. A hierarchy of decision classes provides the ability to represent different decision models.

  Decision steps *conditionally* direct flow from one guideline step to another. GLIF provides a flexible decision model through a hierarchy of decision step classes. The Decision Step allows specification of both deterministic and non-deterministic decisions.

  The decision hierarchy can be extended in the future to model decisions that consider uncertainty or patient preferences. The hierarchy may also be extended to support different decision models.

  Decision steps are nested by specifying a (sub) guideline in the decision_detail attribute of the step. This subguideline is executed before the decision criterion for that step is evaluated. The subguideline would modify or create new variable data items and assign them values. The use of these variables in the decision criteria makes the decision nested. Like the action step, a decision step has attributes that specify its strength of recommendation, strength of evidence,

didactics, iteration information, duration range, triggering events, and associated exceptions.

Choice steps represent a decision between guideline steps for which the guideline does not provide deterministic selection criteria. An external agent, such as a human or another program, must make the decision in choice steps, and select one of the decision options.

The case step provides a means to represent the conditional selection of exactly one path from among several alternatives. The “yes” and “no” options contain expressions of “True” and “False”, respectively, and direct the flow of control to the next guideline steps.

- **Action_Step**

The Action_Step class is used for modeling actions to be performed. Action steps contain tasks. The action specification model includes two types of tasks:

Guideline-flow-relevant actions, such as retrieving data from an electronic patient record, calling a sub-guideline, or computing values for data. They are Subguideline Action, Assignment Action, Generate Event Action, Get Data Object Action, and Get Data For Gel Action.

Clinically relevant actions, such as making recommendations. Clinically relevant actions reference the medical ontology for representations of clinical concepts such as prescriptions, laboratory test orders, or referrals.

In GLIF, guideline encoders specify medical actions by defining the attributes of a Patient Data item according to the data model of the HL7 Reference Information Model (RIM). The HL7 RIM is general enough to represent the data structure for a wide range of medical data and concepts in a uniform manner, while using a small number of classes. Patient data can simply be modeled as *observations*, *medications*, and *procedures*. These classes contain a *mood* code that distinguishes how they can be conceived: as an event that occurred, a definition, intent, order, etc.

The action step has attributes that specify its strength of recommendation, strength of evidence, didactics, iteration information, duration range, triggering events, and associated exceptions. Action Steps can be refined by including a task of Subguideline_Action type in the step. The Subguideline_Action task has a (sub) guideline attribute that contains the nested subguideline. An action step has a *next step* attribute that is used to specify the step to go to once this step has finished execution.

- **Branch_Step**

The Branch_Step and Synchronization_Step allow modeling of multiple simultaneous paths through the guideline.

The branch step is used to model concurrent guideline steps. Branch steps direct flow to multiple guideline steps. All of these guideline steps must occur in parallel. A branch step may link a guideline step to any other guideline step.

- **Synchronization_steps**

Synchronization_steps are used in conjunction with branch steps. When multiple guideline steps follow a branch step, the flow of control can eventually converge in a single step. Each branch may lead to a series of steps, resulting in a set of branching paths. The step at which the paths converge is the synchronization step. When the flow of control reaches the synchronization step, a continuation attribute specifies whether all, some, or one of the preceding steps must have been completed before control can move to the next step. The continuation is expressed as a logical expression of guideline steps (e.g., (Step_A or Step_B) indicates that flow must continue once either Step A or Step B is completed).

- **Patient_State_Steps**

A Patient_State_Step is a guideline step (a node in the flowchart) that is used for two purposes. One purpose is to serve as a label that describes a *patient state* achieved by previous steps. In this way, a guideline may be viewed as a state transition graph, where states are scenarios, or patient states, and transitions between these states are the networks of guideline steps (excluding

patient state steps) that occur between two patient state steps. The other purpose of a patient state step is to serve as an *entry point* to the guideline (e.g., patient came back to the clinic at clinical state A).

3.3.3 Nesting

Nesting allows grouping of parts of a guideline into modular units (subguidelines or macros). This enables partitioning of the guideline parts into units of manageable size that can be comprehended more easily. These modular units can also be reused by other guidelines.

Nesting is very useful for managing complex guidelines. Nesting enables looking at a guideline to be looked at from a top-level view, and then zooming into/out of some of its parts. Nesting is also useful in representing a guideline in the context of other guidelines. Since nesting allows grouping of parts of a guideline into a single unit, it is a mechanism that can allow model extensibility and reuse of parts of a guideline (defining macros), or adaptation of a guideline to a specific institution by replacing specifications for parts of a guideline (i.e., replacing a goal with a procedure).

Decisions are nested by specifying a subguideline in the decision_detail attribute of a decision step. This subguideline is executed before the decision criterion for that step is evaluated. The subguideline would modify or create new variables and assign them values. The use of these variables in the decision criteria makes the decision nested.

Action Steps are nested by including a Subguideline_Action type of task in the step. The Subguideline_Action task has a subguideline attribute that contains the nested subguideline.

Chapter 4

Methodology & System Architecture

Based on the observations and analysis in Chapter 2 and Chapter 3, we present a new practical methodology to build decision models automatically from the knowledge-based GLIF guideline models. We first identify the differences between the DMs and CPGs representations. Then related works are discussed. After that, we will describe in detail our methodology on the CPG-to-DM mapping, including the assumptions, the system architecture, the construction of the DM, and finally the model refinement.

4.1 Comparison of DMs and CPG representations

In recent articles, several authors analyze the differences between the DMs and CPGs [Zhu 2002, Sanders 1998, Hayward 1995, Kamae and Greenes 1991, Margolis 1983, US Congress Office of Technology Assessment 1994]. A DM specifies the probability that a specific clinical situation exists, and quantifies the value of the outcome of a decision. A CPG ideally has this information inherent in its recommendations, but does not represent the information explicitly for the guideline user. Table 4.1 summarizes the main differences between DMs and CPGs [Sanders 1998].

Table 4.1 Comparison of DMs and CPG representations

Decision Models	Clinical Practice Guidelines
Specifies explicitly the probability that a particular clinical state exists	Reflects only implicitly the underlying utilities and probabilities
Quantifies the value of the outcome of a decision	May rely on qualitative reasoning
Answers: (1) Is it more desirable to do A or do B? (2) With what probability is A the most desirable action?	Algorithm prescribes that, given X, do Y
Focuses on pivotal decisions at a local stage	Often deals with multistage workup and management

4.2 Related work

Although researchers have promoted CPG based clinical decision support, they have not done a large amount of work on transforming between DMs and CPGs. Two relatively early studies are work by Shiffman and his colleagues on the use of decision tables to improve clinical guidelines [Shiffman et al., 1992], and work by Kamae and Greenes on the use of a computational model of approximate Bayesian inference for associating clinical algorithms with decision analyses [Kamae and Greenes 1991].

More recently, Sanders [1998], in her PhD work, developed a new approach that allows developers and users to create, disseminate, and tailor CPGs, using normative decision models (represented as decision trees). She proposed that guideline developers use computer-based DMs that reflect known global and site-specific data to generate evidence-based CPGs. In her approach, she defined conceptual models for representing CPGs and DMs, and formalized a system (ALCHEMIST) for mapping

between these two representations. Such CPGs could then be tailored to specific clinical settings, and could also be modified automatically over time as the underlying DM or evidence evolves.

However, her source decision model is only applied to decision trees, and her approach ignores vocabulary issues. The system does not place any restrictions on the naming conventions that the decision analyst uses when he builds the underlying DM. It would affect the integration, sharing and reuse of the system.

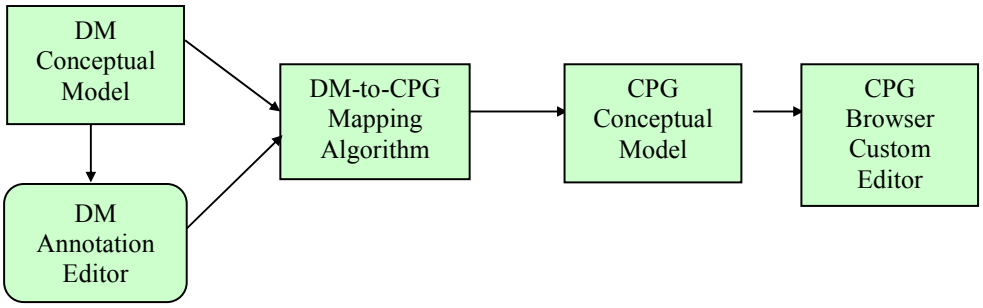

Figure 4.1 Schematic representation of ALCHEMIST's architecture [Sanders 1998]

Another work is by Zhu in her master thesis in 2002. They present a new practical methodology to facilitate effective dynamic decision model construction for evidence-based clinical practice guideline development, updating and customization. The central idea of their methodology is the extraction of the information in existing paper-based CPGs to instantiate a predefined CPG conceptual model (Their CPG conceptual model is based on Sanders' work, 1998). Then the information captured in the CPG conceptual model combined with additional information from other information

sources will be mapped to the Dynamic Decision Model (DDM) conceptual model and instantiated by it. Finally, based on the information of the DDM conceptual model, a DDM is constructed manually and solved to support automated generation of a new computer-based CPG, which may be customized and updated easily and efficiently. The DDM construction is an iterative process, which also requires multiple rounds of input from the additional information sources.

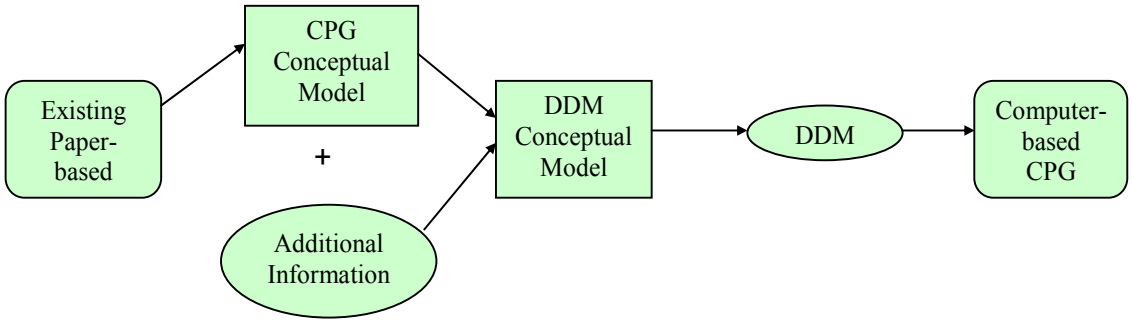

Figure 4.2 Methodology of Zhu's Work [2002]

There are also some guideline-based clinical decision support systems that use the knowledge based structure, like the EON decision support system in Stanford University [Samson et al., 2001], the PRODIGY system in the United Kingdom [Johnson et al, 2000], the ATHENA project in the Veteran's Affairs Palo Alto Clinic [Goldstein et al, 2000]. In their decision models, they implement if-then-else constructs and a form of argumentation – rule-in and rule-out criteria as a way of setting qualitative preferences – for decision making with a non-deterministic choice.

GUIDE [Quaglini et al., 2001] is part of a guideline modeling and execution framework being developed at the University of Pavia. It supports (1) integrating modeled guidelines into organizational workflows, (2) using decision analytical

models such as decision trees and influence diagrams, and (3) simulating guideline implementation in terms of Petri nets (formal model used to model concurrent systems).

GUIDE has a model that uses decision trees or influence diagrams to represent non-deterministic choices. GUIDE provides a link to Java applets that build and use decision trees or influence diagrams that are specific to a situation addressed in a guideline. When a guideline user makes a decision, within a non-deterministic one-of choice, she may select one of the choices or ask for help. When help is requested, a decision tree or influence diagram, the location of which is specified by a URL, can be invoked. Once a decision tree is requested, it must be instantiated with probabilities and utilities. This process is partially automatic (for information that may be stored into a static database table, such as test characteristics, namely sensitivity, specificity and cost). Other data are provided by the EMR or the user through utility assessment tools. These models can be used, for example, to calculate incremental cost-effectiveness or cost-utility ratios. Different considerations such as cost or life expectancy may influence the utility of a choice alternative. The final recommended alternative is calculated based on the expected utility for each possible alternative.

Other relevant representation formalisms include those that incorporate an uncertainty model to a hierarchical representation framework. Some of these efforts attempt to accommodate the uncertainty models by re-interpreting the semantics of existing representations [Lin et al., 1990, Yen et al., 1990], while others try to couple the two to form a coherent framework [Saffiotti 1990]. However, none of these frameworks integrates context-sensitive categorical and uncertainty knowledge in a general way.

4.3 CPG – to – DM Mapping

4.3.1 Assumptions

Before we introduce our new methodology for the DM construction from knowledge-based guideline models, we state some assumptions about the system. First, we assume that there exists one GLIF-based CPG model of high quality judged by the criteria specified by the Institute of Medicine (IOM): validity, reliability, applicability, flexibility, clarity, multidisciplinary process, scheduled review, and documentation [IOM, 1992]. The target problems and target population of the CPG selected are the same as those of the DDM that we intend to construct [Zhu 2002].

Second, in order to simplify the system, we assume that the clinical decision problem could be formulated in a non-dynamic decision model. Although many clinical decision problems are dynamic and take into account the effect of time, we could still represent the time sequence by the occurrence of the nodes. For example,

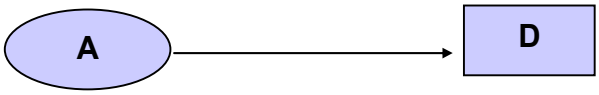

Figure 4.3 Information known before decision is made

Figure 4.3 shows that the outcome of event A is known before carrying out decision D, while from Figure 4.4, we know that decision T is made before decision D.

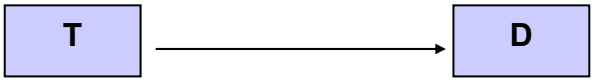

Figure 4.4 Decision T is made before decision D

As such, it is reasonable to assume that non-dynamic influence diagrams could also represent the sequence of the decision problem.

4.3.2 The System Architecture

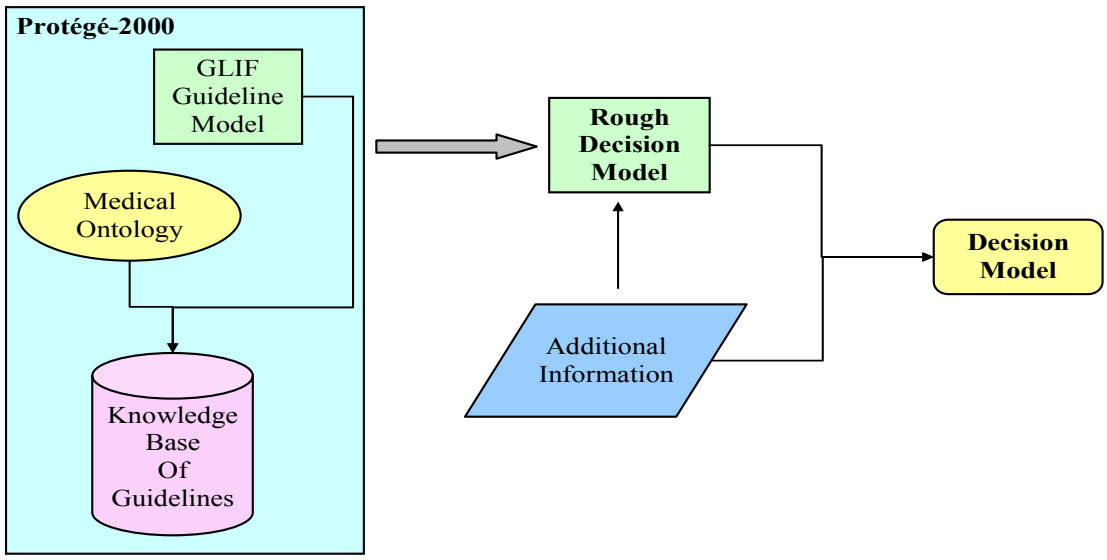

Figure 4.5 Proposed system architecture

Figure 4.5 shows an overview of the proposed system architecture for **ACDMC** (Automated Clinical Decision Model Construction), which is designed to build the rough decision model automatically from the knowledge-based CPG model, and then to refine the decision model by the decision maker with additional information.

4.3.2.1 The knowledge base

Since an ontology typically does not contain instances of concepts, we can view a knowledge base as an instantiation (or an extension) of an ontology. Thus, a knowledge base comprises "filled in" concept descriptions that enumerate the details of the particular application being built. In the ACDMC system for guideline-based medical care, a general ontology defines the general structure of clinical guidelines (the notions of drug therapy, laboratory tests, etc.); the particular knowledge bases on which ACDMC operates define specification for particular guidelines (i.e., individual guidelines for chronic cough, hypertension, thyroid, etc.).

Given domain ontology, knowledge acquisition systems such as Protégé allow straightforward entry of the corresponding knowledge base. The protégé system permits developers to create a domain ontology using a simple editing system. Protégé then uses the domain ontology to create a user interface through which subject-matter experts can enter the detailed content knowledge base. The tools generated by Protégé can also be used to browse and to update the knowledge base as necessary – provided that the overarching domain ontology remains constant.

A guideline modeler uses the Protégé-2000 knowledge-editing environment to create and maintain clinical practice guidelines (CPGs) and protocols. As we introduced in the previous chapter, Protégé-2000 has a frame-based knowledge model: all entities in a Protégé knowledge base – instances, classes, slots, faces, and constraints – are frames. Instances represent objects in the domain of interest (e.g. a patient). Classes are either named collections of instances or abstract conceptual entities in the domain (e.g. the

concept of a drug ingredient). Slots are binary relations describing properties of classes (e.g. the indications of a drug). Faces describe properties of slots (e.g. the data type of a slot's value).

The medical ontology also provides a data model (e.g., Health Level 7's Reference Information Model version 1.0) and a controlled vocabulary (e.g., UMLS) for referencing patient conditions and therapies that are relevant to managing disease. Together with the guideline model, it builds up the knowledge base for clinical decision making.

4.3.2.2 Overview of the Decision Model Construction

Many guideline-based decision models use rule-based criteria as a way of setting qualitative preferences. For example, in hypertension control, if blood pressure is inadequately controlled for less than six months, the guideline leaves the decision to the clinician's judgment. In our method, we envision incorporating expected values computed from a decision-theoretic model to the hierarchical representation framework.

Given a task to automate, the challenge is to construct an appropriate problem-solving method, and to link that problem solver to an ontology that defines the relevant concepts in the application area. Thus in our work, we develop an algorithm to automatically build a *rough decision model* (RDM) from the knowledge base described above. The rough decision model (RDM) is a decision model that is not complete in the structure, or parameters, or both. It is essential to emphasize that this generation

effort should occur within a progressive DM formulation framework. The purpose of such a framework is not to produce an approximately "correct" model but rather to help the decision-maker and his or her teams of experts develop insight about their decision. It is at the formulation phases of the Decision Analysis Cycle (sec. 1.1.2). With the rough model, the decision maker could construct the complete decision model by modifying the rough decision model and filling in additional information like probabilities and utilities.

Our current effort concentrates on analyzing and representing the structure and contents of the clinical decision model. Issues related to other parts of the system, like evaluation of the decision model, will be mentioned without further analysis. Moreover, in this work, the only decision models that we focused on are the *influence diagrams* (IDs). IDs not only provide an explicit representation of probabilistic dependence and independence (compared to decision trees and qualitative probabilistic networks (QPNs)), but also represent the decision variables and preference values (compared to Bayesian networks (BNs)). These characteristics are essential in clinical decision making.

4.3.3 Construction of the Decision Model

The representation of a decision problem can be seen at three levels of specification: relation, function, and number [Howard and Matheson, 1981]. The *relation* level captures the qualitative structure of the problem, as expressed in the topology of the influence diagram. At this level, the arcs specify dependence and independence

between propositions or variables (nodes). IDs at the relation level are similar to several common representations in modeling and AI research, such as semantic nets.

The level of *function* specifies the qualitative functional form of the probabilistic and deterministic relationships among nodes.

The level of *number* quantifies the numeric values in the functions and conditional distributions. For example, at the level of number, we might specify that P(chest pain =mild discomfort | coronary artery disease = 1 vessel) = 0.25.

According to these three levels, our system will automatically generate a rough decision model on the first relation level. In the model refinement stage, with the additional information from the decision maker, the system could complete these three levels.

4.3.3.1 Decision model assumptions

The decision model assumptions [Zhu 2002] include the basic characteristics of the decision problem, and some constraints on the actions, events, and states. In GLIF, the goals/intentions of the CPG are described in text strings in the "Intention" slot of the guideline model [Peleg et al. 1998]. So we map the "Intention" slot to the objective of decision model. The information inherent in the *goals/intentions* of CPG model can help DM developers to decide on the basic characteristics of clinical decision problems (e.g., the problem type, target population).

Furthermore, the overall eligibility criteria of the guideline model usually specify the target population of the disease problem. For example in hypertension, add a second drug guideline (the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) that states the value of the instance of the "eligibility criteria" class is "the patient is not at the goal blood pressure, the response to the initial drug choice for hypertension is inadequate after reaching the full dose, and the patient is tolerating the first choice well". We can see that the target population is clearly identified for this guideline.

Another example in the chronic cough management guideline is that, the objective of the CPG model includes the following information: diagnosis and treatment of chronic cough in immunocompetent adults (people of age >18 years). Chronic cough is defined as cough that lasts 3 weeks or more. Some etiological evidence indicates that chronic cough is due to three coincident diseases 42% of the time [Irwin et al., 1998]. Furthermore, the most common causes of chronic cough are: Postnasal Drip Syndrome (PNDS) (10% to 58%), Asthma (22% to 59%), Gastro esophageal Reflux Disease (GERD) (6% to 21%).

Based on such information, in the DM construction, the problem type may be defined as diagnosis and treatment of chronic cough. The target population is people of age >18 years, immunocompetent, and have cough more than 3 weeks.

4.3.3.2 Mapping Model Structure

With the fundamental problem type, goals, target population specified, and sorted out from the general information of the guideline, we can turn now to the process of structuring the various decision elements – decisions and alternatives, uncertain events and outcomes, and consequences. The system obtains a large portion of the needed information directly from the clinical guideline model. We use the *clinical algorithm* to build the structure of the decision model and map the parameters and ontological contents from the medical ontology. Recall that the steps of the algorithm are subclasses of the Guideline_Step class. Each subclass is used for a step with a different purpose. Each step has a name and associated didactics.

After we load the Clinical Practice Guideline model in GLIF, and medical ontologies, which are information models, the system first initializes an empty influence diagram network. After initializing the ID, the system adds to it the first_step of the flowchart algorithm, and label the first_step as the CurrentStep. As discussed in the previous chapter, the first_step is a Patient_State_Step. In ACDMC's ID representation, this step corresponds to creating a chance node that is related to the patient state. The system creates the ID representation by determining the step type of CurrentStep and performs the actions in detail from a) to d) as follows, until there are no more steps in the flowchart algorithm for the system to traverse. Figure 4.7 gives the algorithm for the structure mapping.

Input: Medical domain knowledge
CPG model in GLIF developed in Protégé-2000 environment
Output: Rough Decision Model

Procedure:
1. Load medical knowledge base (KB) and GLIF clinical guideline model
2. Build the model structure with the CPG flowchart algorithm
2.1 Begin with first_step, connect the nodes with the next_step, Branch_Step, decision options attribute
2.2 node name → name of the step instance
2.3 node type:
chance node → Patient_State_Step (disease info, risk factor, patient info)
decision node → action_step, decision_step (choice / case step)
decision alternatives: decision options attribute
utility node → leave a default value, let the decision maker fill in
2.4 delete Synchronization_Step, Branch_Step (do not consider time issue), connect the parent and child nodes
2.5 extract information from the KB to instantiate the nodes, evidence and support for decision making.
2.6 Traverse the overall flowchart until the end node.
3. Output target rough decision model.

Figure 4.6 Algorithm for the DM structure mapping

a) Patient State Step

The patient state includes all the manifestations, i.e., signs, symptoms, laboratory findings, and complications that are applicable in the example cases [Leong 1990]. Some examples are fever, cough, and bronchospasm. We also classify concepts for describing the general background such as age, sex, drug-abuse-history, and hemophiliac as patient state. These information have close correspondence with the

Chance Node in the decision model, such as disease & background, signs & symptoms, test results, treatment results, treatment complication, follow-up results, and follow-up complication. So if the CurrentStep is a Patient_State_Step, we would map it as a chance node.

Taking the cough study as an example, the algorithm maps the attributes of the GLIF Guideline Model to the DM as the following:

Table 4.2 Attributes mapping from GLIF guideline model to DM

Attributes	GLIF Guideline Model	DM
Name	Chronic Cough	Chronic Cough
ID	CoughStudy_00005	CoughStudy_00005
type	**Patient_State_Step**	**Chance Node**
next_step	Instance (CoughStudy_00010 of Cls(Action_step)) -- Get Patient Cough-related data	connecting information of the network (arc between node "chronic Cough" and "Get Patient Cough-related data")
patient_state_ description	Instance of Cls (Three_ valued_Criterion): Current cough start time, Age, ImmunocompromisedEndTime	general background of patient
Probability	not applicable	assessed by the decision maker or set a default value, such as 0.5

First, we map the value of the name, identity_code attribute from the Patient_State_Step to the Chance node in the decision node, respectively. As we have introduced in the GLIF guideline model in section 3.3.2, next step, branches, and options attributes of the algorithm's guideline steps provide the flow among the steps of the algorithm. We use the value of the next step attribute to connect the nodes "chronic cough" and "get patient cough-related data". The patient_state_description attribute describes the three valued criterion of the state

of the patient: current cough start time, age, and ImmunocompromisedEndTime. These attributes could be further modeled as chance nodes that are connected to the chronic cough node.

b) Action_Step

As we introduced in section 3.3.2.2, the Action_Step has two types of tasks attributes: guideline-flow-relevant actions and medically oriented action. These two types of task specify the details of a clinical action and we could model them as decision nodes. If the tasks belong to the guideline-flow-relevant action classes, such as Assignment_Action_Class, Generate_Event_Action_Class, Get_Data_ Action_Class, we shall model the tasks separately as decision nodes. For example, the Action_Step - Get Patient Cough-related data - in the chronic cough management guideline, contains tasks like get Immunocompromised, get date of birth, get smoking, get PNDS, get pregnancy, get cough, and get ACEI. These tasks involve data related to the patient states, which could be represented as an encapsulated network of disease & background.

If the tasks belong to the medically relevant action classes, such as making recommendations, we can directly map it to the decision node.

c) Decision_Step

The decision step includes Choice_Step and Case_Step. It *conditionally* directs flow from one guideline step to another. So it does not have a “next_step” attribute,

but it has the decision_options attribute. Note that the decision options are not guideline steps. When using Protégé as an authoring tool for GLIF3, decision options are not graphically depicted as flowchart nodes. Instead, they are depicted as connectors.

The value of Decision_options attribute is related to the alternatives of the decision node. The decision options' criteria in a case should be mutually exclusive. If these criteria are not mutually exclusive, and more than one decision option criteria are met, then only one decision option is chosen, arbitrarily.

d) Branch_Step and Synchronization_Step

Since this work does not concentrate on time issues, the Branch_Step and Synchronization_Step, which are used to model multiple simultaneous paths through the guideline, are used only in mapping the qualitative dependence of the variable nodes.

4.3.4 DM Refinement

4.3.4.1 Rationality of the DM

From the rough decision model, the decision maker shall first check the structure of the influence diagram: 1) Whether it represents the decision problem rationally, explicitly, and completely, in both the nodes and their relationships. 2) Representation

requirement of the ID, like the node that no cycles are allowed in the IDs, no-forgetting-arcs, etc.

4.3.4.2 Numerical Parameters

After building the model at a structural (relation) level, the system should assess the numerical parameters, including value functions, conditional probability distributions with additional information from the decision maker.

- **Utility**

As part of modeling a decision problem, the analyst must decide which attributes of the possible outcomes to include in the analysis. In general, a medical decision results in outcomes that affect the attributes of length of life, quality of life, and monetary costs; the utility function to be used in the analysis is an assertion by the analyst of the relevant components of utility in the decision.

- **Probability**

For some events, there can be relevant empirical data to guide probability assessment. But for many real problems, most or all probabilities will need to be obtained from expert judgment [Henrion et al., 1991]. In addition, the decision maker shall take the preferences of the patient into the value function.

4.3.4.3 Level of representation

Since the domain information in the Protégé-2000 knowledge base is organized in a hierarchy of classes, we are able to create IDs at different levels. The level of detail for the decision model is controlled by the user and should take into account the computational cost and the information gathering cost.

In addition, in our decision model, we also support nesting of the decision or chance nodes. Nesting enables a decision model to be looked at from a top-level view and then zooming into/out of some of its parts. Nesting is also useful in representing a sub decision model in the context of the overall decision hierarchy.

Table 4.3 Mapping from GLIF guideline model to DM

<table>
<tr><th colspan="2">GLIF guideline model</th><th>Medical ontology support</th><th colspan="2">Decision model</th></tr>
<tr><td colspan="2" rowspan="2">Goals/intentions (represented as text strings)</td><td rowspan="2">Text material</td><td>Problem type</td><td rowspan="3">decision assumptions</td></tr>
<tr><td>Decision goals</td></tr>
<tr><td colspan="2">Eligibility Criteria of the overall guideline</td><td>Target population</td></tr>
<tr><td colspan="2" rowspan="2">patient state step (structure)</td><td rowspan="4">defining the attributes of a Patient Data item according to the data model of the HL7 Reference Information Model (RIM)</td><td>disease & background</td><td rowspan="2">chance node</td></tr>
<tr><td>signs & symptoms</td></tr>
<tr><td colspan="2">decision step</td><td rowspan="3">test, treatment, follow-up</td><td rowspan="3">decision node</td></tr>
<tr><td rowspan="2">action step</td><td>system action</td></tr>
<tr><td>medical action</td></tr>
<tr><td colspan="2">possible outcomes -- patient state step (structure)</td><td>Patient data item</td><td>test result, treatment outcomes, treatment complications, follow-up outcomes, follow-up complication</td><td>chance node</td></tr>
<tr><td colspan="2">probabilistic & contextual dependencies</td><td>concept relations</td><td>Contextual dependencies from the guideline model. Probability assessed by decision maker.</td><td>arcs and probabilities</td></tr>
<tr><td colspan="2">evaluation criteria</td><td></td><td>cost, morbidity, mortality, quality-adjusted life expectance (QALE),</td><td>utility</td></tr>
</table>

Chapter 5

Case Study

To evaluate the proposed methodology to construct a DM from an existing knowledge-based GLIF guideline model, we have conducted a case study on chronic cough management. This chapter first introduces the background about the clinical problem addressed, and then presents the mapping process.

5.1 Chronic Cough in Immunocompetent Adults

5.1.1 Introduction to Chronic Cough

Cough is consistently among the most common principal reasons for seeing a Physician [Bernstam 2000]. It is generally classified into acute (< 3 weeks) and chronic (lasting 3 weeks or more). Acute cough, though more common and may be accompanied by other serious illnesses, is usually self-limited and does not require evaluation or treatment. Chronic cough, on the other hand, has been shown to adversely affect the quality of life.

5.1.2 Problems in Chronic Cough Diagnosis and Treatment

One of the difficulties with the diagnosis and treatment of chronic cough is that symptoms may be due to more than one cause in a given patient. In fact, statistical data shows that chronic cough is due to three coincident diseases 42% of the time [Irwin et al., 1998]. Furthermore, the common causes of chronic cough are very difficult to diagnose on the basis of history and physical examination.

5.1.3 Notes on Chronic Cough Diagnosis and Treatment

- Although there are many possible causes, the majority of chronic cough instances in immunocompetent adults is caused by post nasal drip syndrome (PNDS), asthma, Gastroesophageal reflux disease (GERD), or a combination of these.

- Chest radiographs should be ordered before any treatment is prescribed in nearly all patients with chronic cough (Grade II-2). Chest radiographs do not have to be routinely obtained before beginning treatment for presumed PNDS in young nonsmokers and pregnant women, or before observing the result of discontinuation of an ACE Inhibitor (ACE-I) for 4 weeks for patients who developed cough shortly after they began to take an ACE-I.

- When the chest X-ray result is normal, PNDS, Asthma, and GERD are the likely causes of chronic cough. In PNDS, sinusitis may be the cause for up to

approximately 30% of the time when the cough is nonproductive, and up to approximately 60% of the time when the cough is productive.

A negative recommendation: Sinus CT scans are not routinely recommended for evaluating sinusitis as the cause of the cough. Four-view sinus radiographs should be ordered instead.

- While 24 hour esophageal pH monitoring is the most diagnostically useful test for assessing GERD as the cause of the cough, conventional indices used by gastroenterologists for assessing esophagitis may be misleadingly normal. Therefore, until future studies provide better guidelines, the test should be read as normal when conventional indices are within the normal range and no suspicious reflux-induced coughs appear during the monitoring session (Grade II-2).

5.2 Case description--Cough Guideline model in GLIF

5.2.1 Purpose of the case study

The main purpose of this case study is to develop a decision model which addresses diagnosis and treatment of chronic cough in people of age greater than 18 years, immunocompetent, and having cough for more than 3 weeks. The decision model is expected to find out the cause of the chronic cough and the corresponding treatment to cure the disease.

5.2.2 Knowledge base used in the case study

For this case study, the knowledge bases that we use are:

- *Chronic Cough management guideline modeled in GLIF*. The selected guideline was from *ACP (*American College of Physicians – American Society of Internal Medicine's guideline for managing chronic cough), since it addresses the same clinical problem (chronic cough) that we intend to deal with.

- *Chronic Cough domain ontology* provides a data model and a controlled vocabulary for referencing patient conditions and therapies that are relevant to managing chronic cough.

5.2.3 File format of the knowledge-based guideline model

5.2.3.1 Brief introduction on XML

The GLIF guideline model and domain ontology contain the chronic cough guideline knowledge base. They are both modeled and maintained in the Protégé-2000 environment. As we described previously, the guideline model in Protégé-2000 could be saved in XML format. XML stands for the **eXtensible Markup Language** (http://www.w3c.org/xml), a notation for marking up the content of documents. It is widely considered to be fundamental to the movement of content-rich documents across the internet, and to be a core technology for the Semantic Web, e-science and scientific Grids. The World Wide Web Consortium (W3C) recently adopted XML as a

standard and several major software vendors (including Microsoft, Sun Microsystems, Netscape, Adobe, and IBM) support XML. XML documents can be viewed in current web browsers and there are a rapidly increasing number of tools for handling XML documents. The major programming languages also have an application programming interface (API) for processing XML documents.

Efforts are also underway to incorporate XML into widely used health care standards such as HL7. The Protégé team developed the XML Backend as the default storage format of Protégé files. Kahn et al. also explored the use of XML to mediate between components of the computer-based patient record (CPR) and sought to integrate existing web-based systems for structured reporting (SPIDER) and probabilistic decision support (BANTER) [Kahn et al, 1998].

In addition, there exists some special tools for the XML file transformation, Xalan, which is an XSLT (a language for transforming xml files) processor for transforming XML documents into HTML, text, or other XML document types. It contains operators for selecting nodes from the tree, using templates to filter out the information, reordering the nodes, and outputting nodes.

5.2.3.2 XML based Bayesian network format

Over the last several years, there has been ongoing discussion of the potential value of creating a ***Bayesian Network Interchange Format*** **(BNIF)** to enhance the exchange of knowledge and experimental results in the community in the Uncertainty and Artificial Intelligence (UAI) community (http://www.uai.org). During the 1998 Conference on

UAI in Madison, Wisconsin, there was a panel discussion about the future of the BNIF. The discussion converged on the value of leveraging XML to revitalize the BNIF efforts. Later, several research groups proposed formats on the XML-based BN, including XMLBIF (**XML**-based **B**ayesNets **I**nterchange **F**ormat), developed by Fabio Cozman et al (http://www-2.cs.cmu.edu/~fgcozman/Research/ Interchange Format/), and **XBN** (for "Bayesian network in XML"), developed by the DTAS group at Microsoft Research (http://www.research.microsoft.com/ dtas/bnformat/).

The XMLBIF format is being implemented in the **JavaBayes** (http://www-2.cs.cmu.edu/~javabayes/), **GeNie** systems and **BNJ** (http://bndev.sourceforge.net/history.html); there have been signs that implementations in the Netica and Hugin systems are in the works.

As such, we use the cough guideline model saved in XML format as the input of our system. It includes the following files: core_GLIF, Cough Study, Data_Model (RIM_USAM), Diagram, GLIF 3.4, Global Concepts, User defined instance ontology. It is available online at (http://smi-web.stanford.edu/projects/intermed-web/guidelines/GLIF1.htm) Figure 5.1 shows a screenshot of the knowledge model file.

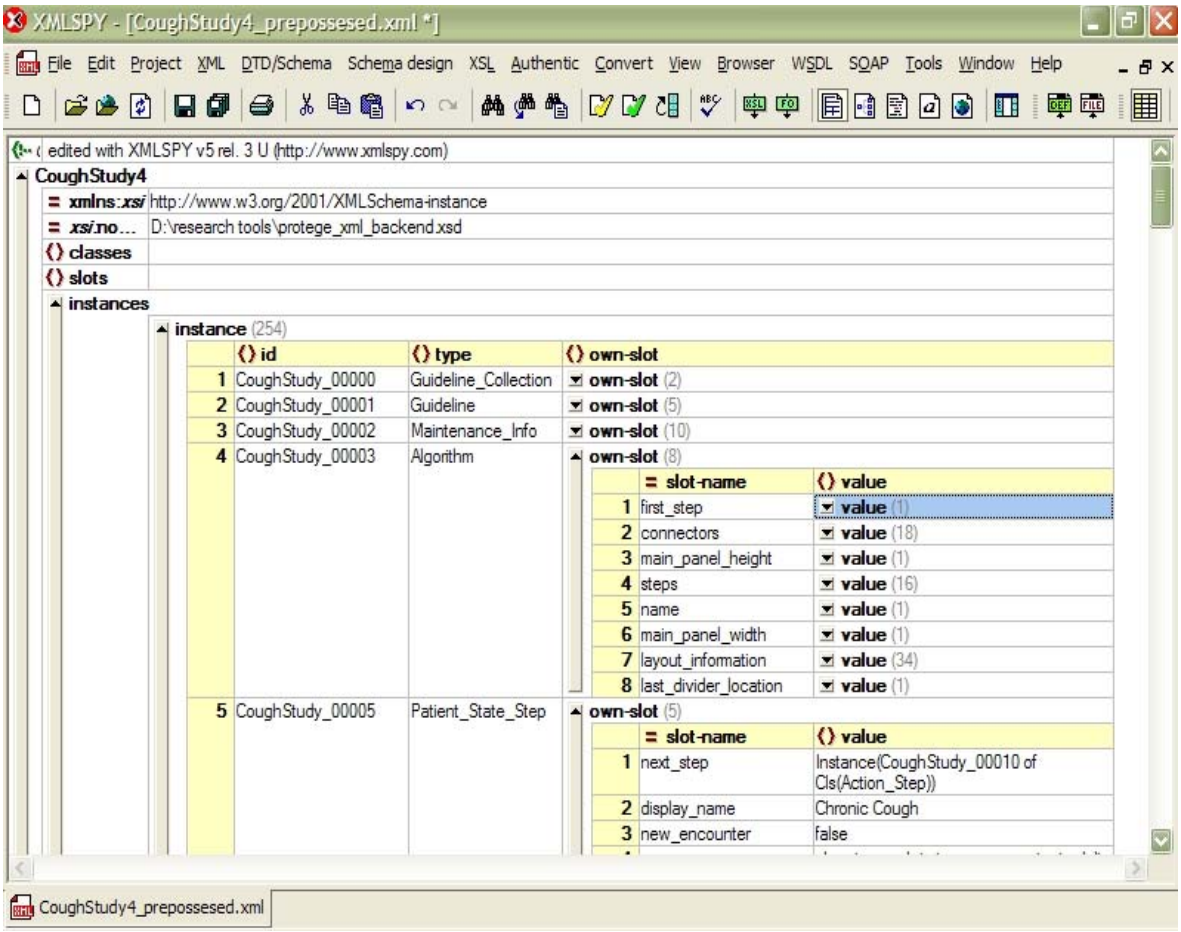

Figure 5.1 Screenshot of the knowledge model in xml format

In addition, we extend the XMLBIF to **XML-based Influence Diagram** (**XMLID**), as the format of our output decision model. The details of XMLBIF, including the description of the format, DTD file (Document Type Description), and examples could be found at the website: http://www-2.cs.cmu.edu/~fgcozman/Research/Interchange Format/. The DTD file for the XMLID format is shown in Figure 5.2.

```
<!-- DTD for the XMLID format -->
<!DOCTYPE XMLID [
    <!ELEMENT XID (NETWORK)*>
        <!ATTLIST XID VERSION CDATA #REQUIRED>
    <!ELEMENT NETWORK (NAME, (PROPERTY | VARIABLE |
PROBABILITY)*)>
    <!ELEMENT NAME (#PCDATA)>
    <!ELEMENT PROPERTY (#PCDATA)>
    <!ELEMENT TYPE (#PCDATA)>
    <!ELEMENT VALUE (#PCDATA)>
    <!ELEMENT VARIABLE (NAME, (VALUE | PROPERTY)*)>
        <!ATTLIST VARIABLE TYPE (chance | decision | utility) "chance">

<!-- topological dependency structure information -->
    <!ELEMENT STRUCTURE (ARC|MEMBER)*>
 <!-- specify dependency arc -->
    <!ELEMENT ARC EMPTY>
        <!ATTLIST ARC
      PARENT NMTOKEN #REQUIRED
      CHILD NMTOKEN #REQUIRED>
 <!-- specify set inclusion for parentless variables -->
    <!ELEMENT MEMBER EMPTY>
         <!ATTLIST MEMBER NAME NMTOKEN #REQUIRED>

<!-- specify probability -->
    <!ELEMENT PROBABILITY (FOR | GIVEN | TABLE | ENTRY |
DEFAULT | PROPERTY)*>
    <!ELEMENT FOR (#PCDATA)>
    <!ELEMENT GIVEN (#PCDATA)>
    <!ELEMENT TABLE (#PCDATA)>
    <!ELEMENT DEFAULT (TABLE)>
    <!ELEMENT ENTRY (VALUE*, TABLE)>
```

Figure 5.2 DTD file for XMLID

The system described here could also be extended to incorporate client-side Java software for data entry and inference. XML has the potential to facilitate the integration of data entry, decision support, and other components of the evolving computer based patient records.

5.2.4 Chronic Cough Management DM Formulation

To begin with our ACDMC system's DM construction process for chronic cough, we first map the information of the GLIF guideline model to the decision model assumptions. Since in the GLIF, goals and intentions are described as text strings in the "Intention" slot of the guideline, we could have:

Problem type: diagnosis and treatment of chronic cough.

Target population: people of age >18 years, immunocompetent, and have cough for more than 3 weeks.

Evaluation Criteria: Cost/effectiveness, quality-adjusted life expectance (QALE).

Next, we proceed to the mapping of the decision model structure. We use the influence diagram representation of the DM. Recall that an influence diagram is a directed, acyclic network of 4 kinds of nodes, i.e., decision node, chance node, deterministic node, and value node. We use the step class, subclass of the clinical algorithm class, to form the top level structure of the influence diagram. Figure 5.3 shows the flow chart of the top level cough management algorithm, and the Treatment of cough is modeled as a subguideline as represented in Figure 5.4. The starting-point of the diagram is mapped from the first_step of the algorithm, which is a Patient_State_Step. The details of the mapping from Patient_State_Step (Chronic cough) to Chance node (chronic cough) are shown in Table 5.1. The

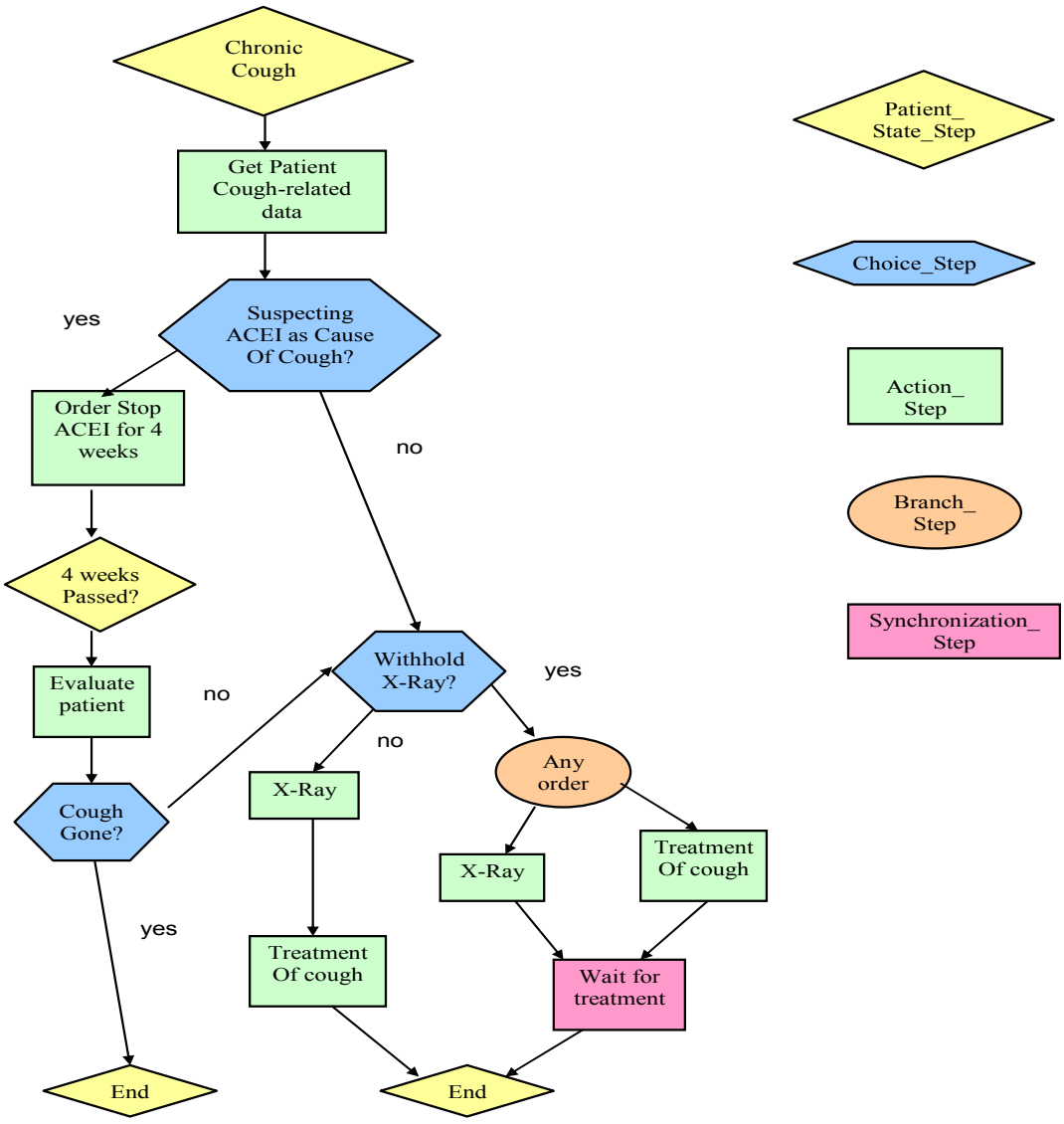

Figure 5.3 The top-level cough management algorithm.

- Description of Figure 5.3

  First, relevant patient data is collected in an action step. Then we decided whether "suspecting ACEI as the cause of cough" (a choice step). If ACEI is suspected to be the cause of cough, then we order to stop the ACEI through the action step "Order stop ACEI for 4 weeks" that has a medically-oriented action specification task. At the time that the order to stop ACEI is given, the current time is assigned

to the variable “time_ACEI_stopped”. This will be used to determine the time of 4 weeks after ordering to stop ACEI, in the patient state step -- "4 weeks passed?".

The patient is sent home for 4 weeks. If 4 weeks passed, then the patient is evaluated through the action step “Evaluate patient”. This action has a Get_Data task that queries for the status of the latest Cough. This action step follows a patient state step that marks a state of at least 4 weeks after the patient was taken off ACEI. Instead of using a patient state step, the action step of ”Evaluate patient” can be triggered by an event that signals that 4 weeks passed, as shown in the action step’s triggering_events slot. Having a triggering event means that we monitor for the event and when it occurs, we trigger the action step. It is different from having the patient come in for a visit and then matching his state to the entry points of the guideline (the patient state steps).

After the patient is evaluated, and the latest Cough value is taken, we can ask if the cough is gone. This is done via a choice step that has two options: “yes” and “no”. The Rule-in for the “yes” option is shown below. Now that we have observed the patient for 4 weeks we can go on to the rest of the guideline. The next step is a user choice step. The user needs to decide whether there are reasons to withhold the X-Ray or not. If we need to withhold the X-Ray, we perform the X-Ray and the Treatment sub-guideline in any order and then wait until the “Treatment” action is executed before we end the guideline. Otherwise, we perform them in sequence.

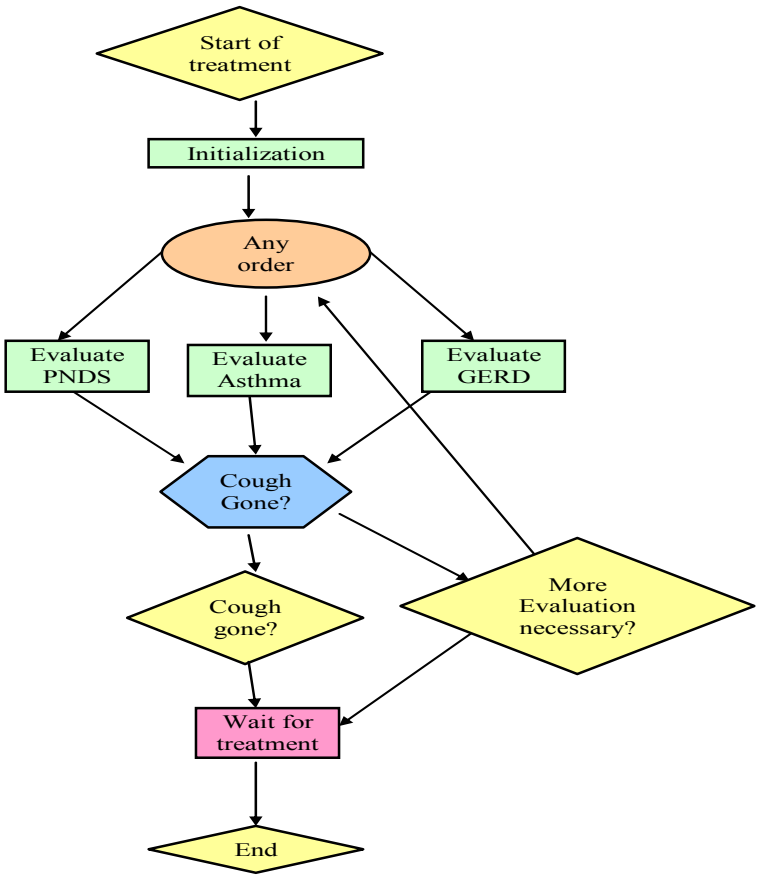

Figure 5.4 The treatment of cough algorithm.

- Description of Figure 5.4

  The "Initialization" action step is used to initiate the values of flags that specify whether PNDS was evaluated, GERD was evaluated, and Asthma was evaluated. The treatment sub-guideline lets the user execute the 3 evaluation actions in any order. Synchronization occurs after the cough is resolved, or after all three evaluation action steps were executed. The user should decide whether the test results are normal. When an evaluation step is executed, the appropriate flag is set to "True". The automatic case step "more evaluation necessary" checks to see whether one of the evaluation flags signals that an evaluation was not done yet. Its result matches "True" or "False" and this determines the traversal of the algorithm.

Table 5.1 The mapping of Patient_State_Step to Chance Node

Attributes	GLIF Guideline Model	DM
Name	**Chronic Cough**	**Chronic Cough**
ID	CoughStudy_00005	CoughStudy_00005
type	**Patient_State_Step**	**Chance Node**
next_step	Instance (CoughStudy_00010 of Cls(Action_step)) -- Get Patient Cough-related data	connecting information of the network (arc between node "chronic Cough" and "Get Patient Cough-related data")
patient_state_ description	Instance of Cls (Three_ valued_Criterion): Current cough start time, Age, ImmunocompromisedEndTime	general background of patient
Probability	not applicable	assessed by the decision maker or set a default value, such as 0.5

Since the *Next_step*, *branches*, and *options* attributes of the algorithm's guideline steps provide the flow among the steps of the algorithm, we catch the information of these attributes of the steps to generate the arcs of the influence diagram.

Then we perform the actions detailed in 4.3.3.2, for the mapping of the action_step and the decision_step (choice_step / case_step) to a decision node, until there are no more steps in the clinical algorithm for the system to traverse. Tables 5.2 -5.3 are some examples of the mapping. Figure 5.5 shows the nested representation of the decision node generated from action_step "Get Patient Cough-related data".

Table 5.2 The mapping of Action_Step to Decision Node

Attributes	GLIF Guideline Model	DM
Name	**Get Patient Cough-related data**	Get Patient Cough-related data
ID	CoughStudy_00010	CoughStudy_00010
type	**Action_Step**	**Decision Node**
next_step	Instance (CoughStudy_00107 of Cls(Choice_step)) -- Suspecting ACEI as cause of cough?	Connecting information of the network (arc between node "Get Patient Cough-related data" and "Suspecting ACEI as cause of cough?")
tasks	Get Immunocompromised	The content of the tasks relate to the patient background, signs and symptoms of the disease, so it could be represented as a nested network in the decision model.
	Get Date Of Birth	
	Get Smoking	
	Get PNDS	
	Get Pregnancy	
	Get Cough	
	Get ACEI	

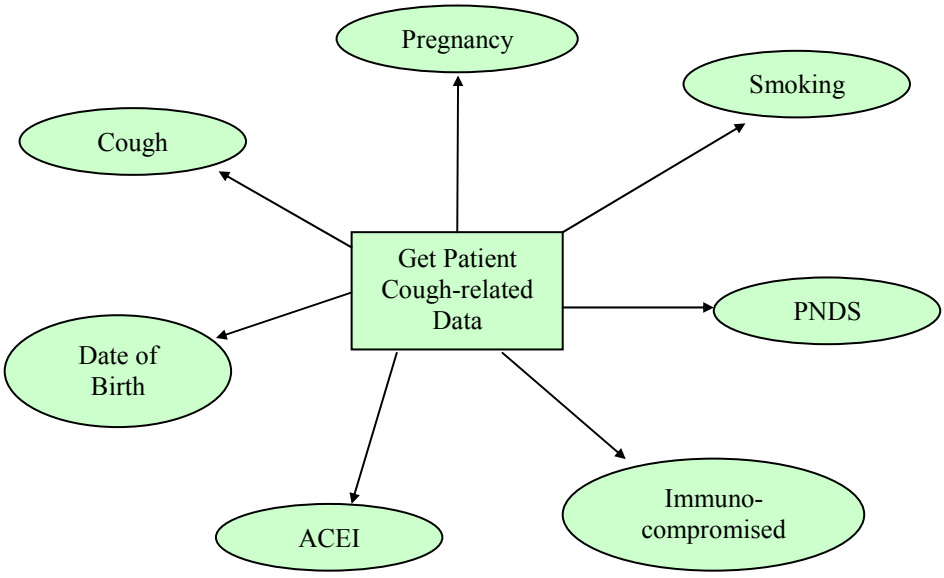

Figure 5.5 The nested representation of the decision node

Table 5.3 The mapping of Decision_Step (choice/case step) to Decision Node

Attributes	GLIF Guideline Model	DM
Name	**Suspecting ACEI as cause of cough?**	Suspecting ACEI as cause of cough?
ID	CoughStudy_00107	CoughStudy_00107
type	**Choice_step**	Decision Node
options	CoughStudy_00122 of Cls (Decision_Option) – No CoughStudy_00122 of Cls (Decision_Option) – Yes	Decision alternative: "Yes" or "No".
	destination attribute of "Yes" and "No"	connecting information of the network (arc between node "chronic Cough" and "Get Patient Cough-related data")

After parsing the whole cough management algorithm, we could get a rough decision model as shown in Figure 5.6. It may not be a complete model and may even not be a valid ID, but it represents the overall structure of the decision problem. Our case study of chronic cough is comparatively simple, but many other decision problems in the medical domain are rather complex and involve a huge amount of nodes and arcs. So the top level ID could give a neat view of the structure and the decision maker may refine the model with different levels of representation. In addition, we illustrate the rough decision model in XMLID in Appendix A.

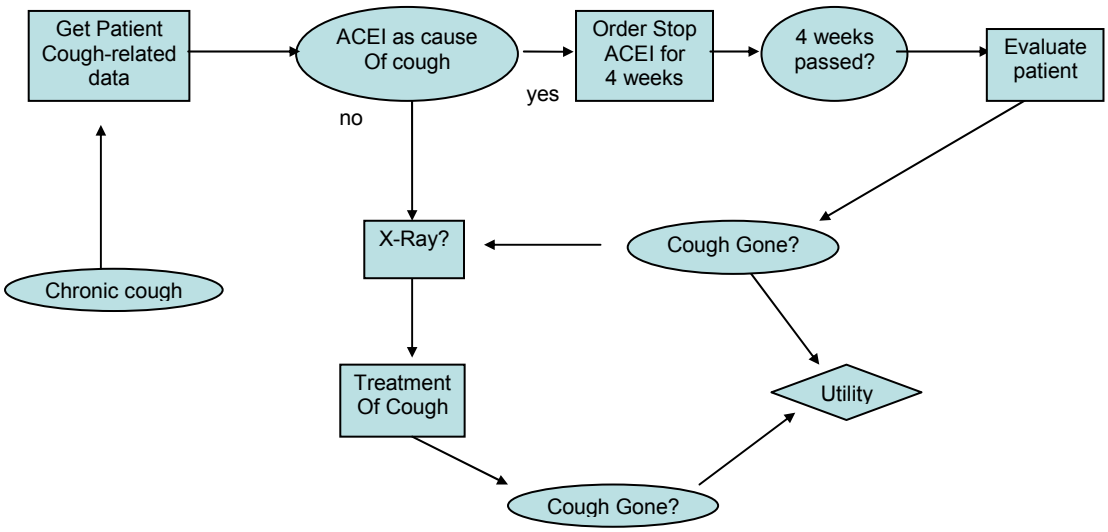

Figure 5.6 The rough decision model

The knowledge base usually contains a lot of information. The domain knowledge are modeled in a hierarchical structure, and they are also linked with the concept relationship class in Protégé-2000 environment. If we want to get a more detailed DM, we could choose other levels of representation other than the top level. The lower levels are instantiated with more instance supports of the domain ontologies. Accordingly, the network is much bigger. Figure 5.7 illustrated the chronic Cough DM after being refined with more information from the knowledge base.

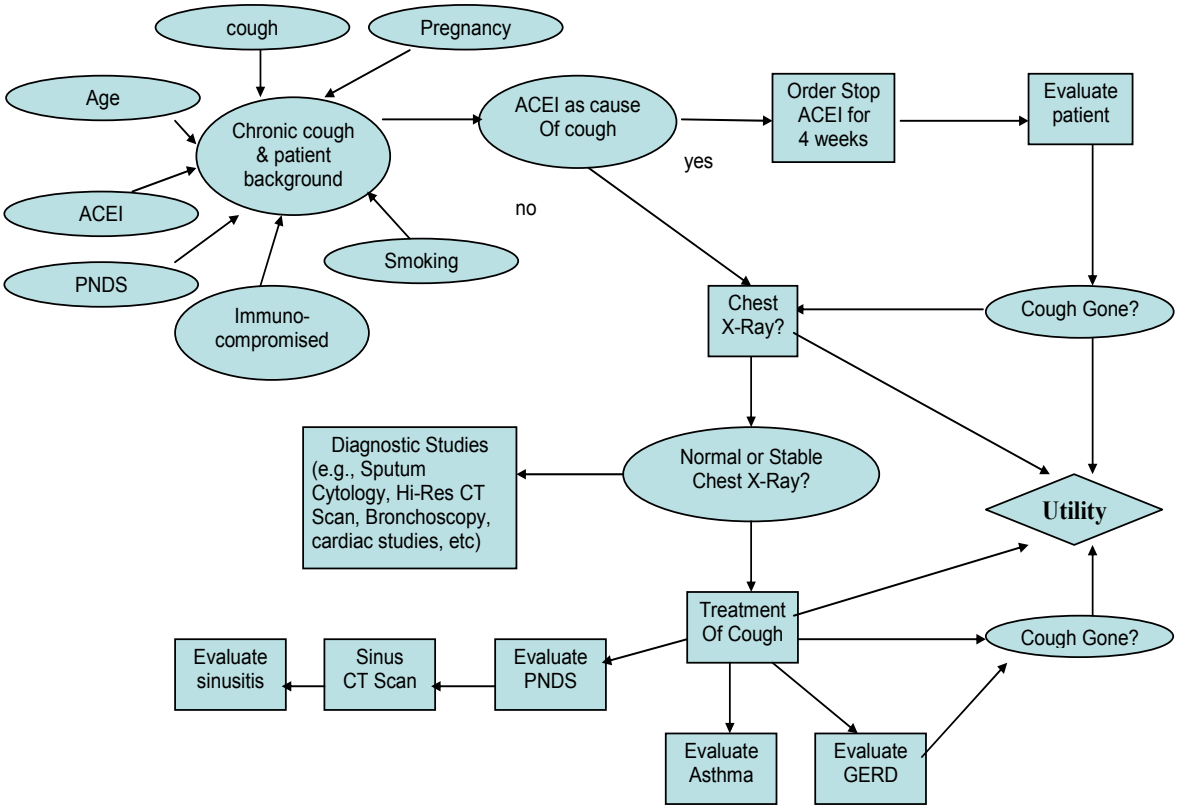

Figure 5.7 Refined model

Chapter 6

Conclusion

6.1 Summary

This work presents a new approach to support automated construction of clinical decision models from a knowledge base. The methodology aims to facilitate application of the decision analysis paradigm in clinical domains. We make use of the knowledge-based CPG model in GLIF format as the input knowledge model. Together with the medical ontologies, which provide structured data models and controlled vocabularies for referencing patient conditions and therapies that are relevant to managing disease, it builds up the knowledge base for clinical decision making.

We develop an algorithm to automatically build a *rough decision model* (RDM) from the knowledge base described above. The RDM is a decision model that is not complete in the structure, or parameters, or both. However, it gives a neat view of the decision problem with the information extracted from the knowledge base. Rule-based references are widely used in many guideline-based decision models. We incorporate expected values computed from a decision-theoretic model to the hierarchical

representation framework. In addition, it greatly reduces the efforts needed for constructing a decision model manually. With the rough model, the decision maker could construct the complete decision model by modifying the RDM and filling in additional information like probabilities and utilities.

6.2 Contributions

Our work facilitates the clinical model construction from the knowledge-based GLIF guideline system. It greatly reduces the huge amount of work needed for building the clinical DM.

We also use the controlled vocabulary and structured data models, like HL7-RIM, to develop the decision model. It will ease the reuse and exchange of the DMs among different hospitals and institutes.

In addition, the knowledge-based decision model will enable the support of information about CPGs and medical ontologies to be stated explicitly. The users will have a better understanding of reasons why specific options are better than others. It gives the users more flexibility in following local practices when existing recommendations support these practices.

Another advantage of this model is the ease in representing changes for updating CPGs. When there are changes in disease prevalence or when new technology becomes available, it would be easier to update information in the model.

6.3 Limitations

Our current effort concentrates on analyzing and representing the structure and contents of the clinical decision model. In addition, we use the sequence of the nodes to represent the temporal precedence. However, many clinical decision problems are dynamic and need to encode time as a very important element. Thus, our system is not suitable for those problems. Dynamic decision models, like Markov decision process (MDP), need to be developed.

6.4 Future Work

The interesting topics in future work include the following:

6.4.1 Evaluation of the decision model

We save our target decision model in the XMLID (XML-based Influence Diagram) format. In the next step, we plan to transform the DTD file to XML Schema, which itself is in XML format. Then we will evaluate the ID model in JavaBayes (http://www-2.cs.cmu.edu/~javabayes/), GeNie (http://www2.sis.pitt.edu/~genie/), or other software supporting the XMLID format.

6.4.2 Extend the current decision model to a dynamic DM

Certain clinical conditions require modeling of repetitive events or modeling of patients at continuous risk. As discussed in the last section, a limitation of our system is that it cannot precisely represent the temporal sequence. So we plan to extend the current decision model to a dynamic decision model, like a Markov Decision Process. A Markov model (in the medical domain) is a type of state-transition model in which the transition probabilities depend on only the current patient state. It is one method in which we can model time dependence and improve our framework.

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Appendix A

Rough Decision Model in XMLID Format

```
<?xml version="1.0" encoding="UTF-8"?>

<!DOCTYPE XID "XMLID.dtd">

<XID VERSION="0.1">
    <NETWORK>
        <NAME>Chronic_Cough</NAME>
        <!-- Variables -->
        <VARIABLE TYPE="chance">
            <NAME>Chronic_Cough</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>Present</VALUE>
            <VALUE>Absent</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="decision">
            <NAME>Get_Patient_Cough_related_data</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>Get_Date_of_Birth</VALUE>
            <VALUE>Get_Smoking</VALUE>
            <VALUE>Get_Sex</VALUE>
            <VALUE>Get_Cough</VALUE>
            <VALUE>Get_PNDS</VALUE>
            <VALUE>Get_ACEI</VALUE>
            <VALUE>Get_Pregnancy</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="chance">
            <NAME>Pregnancy</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>True</VALUE>
            <VALUE>False</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="decision">
            <NAME>Suspecting_ACEI_as_cause_of_cough</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>True</VALUE>
            <VALUE>False</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="decision">
            <NAME>Order_Stop_ACEI_for_4_weeks</NAME>
            <TYPE>discrete</TYPE>
            <VALUE> Order_Stop_ACEI </VALUE>
        </VARIABLE>
```

```
        <VARIABLE TYPE="decision">
            <NAME>Evaluate_patient</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>Evaluate_Cough</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="chance">
            <NAME>4_weeks_passed</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>True</VALUE>
            <VALUE>False</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="decision">
            <NAME>Evaluate_Patient</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>Evaluate_Cough</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="chance">
            <NAME>Cough_Gone_1</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>True</VALUE>
            <VALUE>False</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="decision">
            <NAME>Treatment_of_Cough</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>Evaluate PNDS</VALUE>
            <VALUE>Evaluate Asthma</VALUE>
            <VALUE>Evaluate GERD</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="decision">
            <NAME>XRay</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>chest_Xray</VALUE>
        </VARIABLE>

        <VARIABLE TYPE="utility">
            <NAME>Utility</NAME>
            <TYPE>discrete</TYPE>
            <VALUE>Utility table</VALUE>
        </VARIABLE>

    <!--Structure specify dependency arc-->
    <STRUCTURE>
      <ARC PARENT="Chronic_Cough" CHILD="Get_Patient_Cough_related_data"/>
      <ARC PARENT="Get_Patient_Cough_related_data"
CHILD="Suspecting_ACEI_as_cause_of_cough"/>
      <ARC PARENT="Suspecting_ACEI_as_cause_of_cough"
CHILD="Order_Stop_ACEI_for_4_weeks"/>
      <ARC PARENT="Suspecting_ACEI_as_cause_of_cough" CHILD="XRay"/>
      <ARC PARENT="Order_Stop_ACEI_for_4_weeks" CHILD="4_weeks_passed"/>
      <ARC PARENT="4_weeks_passed" CHILD="Evaluate_patient"/>
      <ARC PARENT="Evaluate_patient" CHILD="Cough_Gone"/>
      <ARC PARENT="Cough_Gone" CHILD="XRay"/>
      <ARC PARENT="XRay" CHILD="Treatment_of_Cough"/>
      <ARC PARENT="Treatment_of_Cough" CHILD="Cough_Gone_1"/>
```

```
        <ARC PARENT="Cough_Gone" CHILD="Utility"/>
        <ARC PARENT="Cough_Gone_1" CHILD="Utility"/>
    </STRUCTURE>

    <!-- Probability distributions -->
        <PROBABILITY>
            <FOR>Chronic_Cough</FOR>
            <TABLE>0.5 0.5 </TABLE>
        </PROBABILITY>

……

    </NETWORK>
</BIF>
```