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ASTI: A Guideline-based Drug-Ordering System for Primary Care

Brigitte Séroussi[a], Jacques Bouaud[a], Hervé Dréau[b], Hector Falcoff[c], Christine Riou[d], Michel Joubert[e], Christian Simon[f], Gérard Simon[g], Alain Venot[b]

[a] *Service d'Informatique Médicale, DSI/AP-HP, Paris, France*
[b] *EA 2494, Faculté de Médecine Cochin Port-Royal, Université Paris 5, France*
[c] *SFTG, Paris, France*
[d] *LIM, Université de Rennes 1, France*
[e] *LERTIM, Université de la Méditerranée, Marseille, France*
[f] *Silk-Informatique, Angers, France*
[g] *RESIP, Boulogne sur Mer, France*

Abstract

Existing computer-based ordering systems for physicians provide effective drug-centered checks but offer little assistance for optimizing the overall patient-centered treatment strategy. Evidence-based clinical practice guidelines have been developed to disseminate state-of-the-art information concerning treatment strategy but these guidelines are poorly used in routine practice. The ASTI project aims to design a guideline-based ordering system to enable general practitioners to avoid prescription errors and to improve compliance with best therapeutic practices. The « critic mode » operates as a background process and corrects the physician's prescription on the basis of automatically triggered elementary rules that account for isolated guideline recommendations. The « guided mode » directs the physician to the best treatment by browsing a comprehensive guideline knowledge base represented as a decision tree. A first prototype, applied to hypertension, is currently under development.

Keywords:

Drug prescription, physician order entry systems, clinical practice guidelines, decision support, primary care.

Introduction

Several studies [1-2] have demonstrated that the use of drugs by physicians is often inadequate both in outpatient settings and in hospitals. Medication errors are common and may cause potentially serious injuries.

Prescribing errors may be classified into two categories. The first concerns errors such as incorrect dose, drug interactions or contraindications, and corresponds to either incorrect use of a drug, or an inappropriate combination of drugs. The second type of error involves the choice of an inappropriate therapeutic strategy leading, for instance, to the prescription of an inadequate drug or to the non prescription of the most appropriate drugs.

Computerized physician order entry (POE) systems have already proved to be efficient tools for improving the safety of drug prescriptions and for preventing the first type of error [1-4]. Several checks are indeed implemented within drug databases that help the physician to select correct drug doses and to detect drug interactions, allergies and, more generally, all contraindications due to the condition of the patient. These functions are now available in hospital information systems and in software for use by the physician in primary care.

However, providing drug-centered recommendations is not effective to promote best patient-based therapeutic strategies and to avoid the second type of error. Interest has recently increased in the development of evidence-based clinical practice guidelines (CPGs) to disseminate state-of-the-art medical knowledge among physicians. The dissemination of CPGs via the internet in text form has not been shown to have an effect on the ordering behavior of physicians. If implemented within decision support systems, the integration of CPGs into the routine workflow of patient care remains a critical obstacle to their effective use.

In this paper, we describe ASTI[1] (« Aide à la Stratégie Thérapeutique Informatisée ») a French national research project that aims to develop a decision-support system applied to prescribing practice in primary care. The system is being developed to provide guideline-based support for prescription writers to prevent both types of medication error, thereby improving existing software. It is integrated into an electronic medical record (EMR) and is built upon a drug database designed to check for errors of the first type.

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[1]ASTI is a 2.5-year project, partially funded by the French Ministry of Research and Technology, which has started in January 2000.

Guideline information has been embedded to improve therapeutic strategy recommendations, thereby avoiding errors of the second type.

The system can be used in two modes: (i) the « critic mode » which operates as a background process, monitoring the physician's prescriptions and querying the physician's proposal if better alternative medication is available, (ii) the « guided mode » in which the physician is voluntarily involved in the search for the best patient-specific treatment recommendation, with no prior prescription. In both modes, the physician makes his own choice and can override any system suggestions.

In the following section, we will recap on the main approaches developed for POE systems for improving the therapeutic strategies of physicians. We will then describe the two utilization modes of ASTI, principles for implementation and the architecture of the system. An example will be developed, illustrating the successive steps and the information processing sequence. Finally, the benefits and drawbacks of the approaches developed are discussed in the last section.

Computer-based prescription ordering systems to improve therapeutic strategy

As early as in the 1970s, efforts were made to design expert systems for improving the therapeutic strategy in a given domain. More recently, CPGs have been widely developed and disseminated to improve the compliance of physicians to standards of good care. CPGs embedded in decision support systems should provide, at the point of care, state-of-the-art, patient-specific evidence-based recommendations. In practical terms, computerized guideline-based physician ordering systems appear to be « comprehensive » EMRs. When the physician enters a new prescription after inputting patient data into the EMR, certain messages may be displayed in alert windows. These messages may be generated by drug database daemons responsible for checking the overall consistency of the physician's prescription in a drug-centered way. These alerts may also be triggered by simple guideline-based rules acting as patient-specific reminders.

However, to optimize the overall therapeutic strategy for a given patient, it is necessary to take into account the whole picture of his disease management and thus to consider complex guidelines, involving the more professional interpretation of patient data, which rule-based approaches cannot provide. These limitations have led to the development of formalisms combining rule-based and task-based paradigms to represent clinical processes. From the Arden Syntax to PROforma [5], GLIF [6], EON [7], and Asbru [8], various guideline representation formats have been proposed.

The PRODIGY project is close to ASTI both in spirit, (the design of a guideline-based prescribing decision-support system), and in target system users, (general practitioners or GPs). This project is being developed in the UK from commercially available EMRs. In phases I and II [9], the system operated on the basis of automated triggering of the appropriate clinical recommendation from the input of a Read Code to describe a patient's disease. The system was judged to be inadequate for chronic disease, and therefore the development of patient scenario [10] to drive the decision-making process was added in phase III. Phases I and II are similar to ASTI critic mode, and phase III implements a guideline model along with interacting modes that are similar to the guided mode of ASTI.

The ASTI system

The objectives of the ASTI system are to provide a higher level of support for POE than is provided by available systems by integrating patient clinical information, drug database information and guideline information into the routine workflow to help physicians to avoid both types of error and to make them aware, at the point of care, of the best patient-specific treatment practices.

User Interaction Patterns

Information about treatment strategy is provided to the prescriber in ASTI via two modes, responding to different needs in prescription support.

In the « critic mode », ASTI operates downstream from the order-entry phase. The physician has to organize his prescription to record each medication order along with the disease or symptom that motivates the prescription using ICD10 concepts. Then, on the basis of the total prescription, the system interprets the physician's therapeutic strategy and, if necessary, delivers alerts, criticisms and evidence-based alternative recommendations, if available. The objective of this mode is to prevent suboptimal or erroneous prescriptions.

In the « guided » mode, ASTI operates upstream from the prescription process. This approach has been successfully tested in routine use with the OncoDoc system [11], applied to the management of breast cancer patients. The physician specifies the disease to be treated and is then "guided" through a knowledge base to obtain the most appropriate patient-specific treatment recommendations. These may serve as a prescription pattern for the order-entry system.

Implementation Principles

The patient model

The role of the patient model in ASTI is to provide a representation of patient information to be used by the other modules at a level of abstraction consistent with guideline knowledge. This representation is built from the patient data available in the EMR. It comprises raw data, either quantitative (e.g. $Cl_{creat} = 60$ ml/mn) or qualitative (ICD10-code = I10, for hypertension), and derived data (renal-function = good) inferred through encoded interpretation rules (if $Cl_{creat} > 50$ ml/mn then renal-function = good). The resulting representation includes demographic data, lab results, diseases, and so on, but also the history of drugs previously administrated indexed according to their reason for prescription.

The patient model uses conceptual graph formalism [12] as its core representation, facilitating abstraction processes based on subsumption. Thus, ASTI aims to use existing hierarchical classifications for abstraction and reasoning using patient-specific information. The ICD-10 hierarchy for diseases and the ATC (Anatomical, Therapeutical and Chemical) classification for drugs constitute the main components of the model ontology. This ontology must be extended to account for the notions on which CPGs are based which have no counterparts in available thesauri or hierarchies. However, whereas ontological reasoning is part of the formalism, additional interpretation rules are encoded as IF-THEN rules that match some data to derive more abstract representations.

Critic Mode

The role of the critic mode is to make constructive criticisms of a user's prescription entered in the POE system, when appropriate and when possible, with respect to an identified therapeutic problem and to an abstract model of both the current state and history of the patient, derived from data contained in the EMR.

The first step is the abstraction of the user's prescription, that is, the generalization of the therapeutic strategy to a level compatible with guideline recommendations. The second step is the identification of candidate guideline rules that apply to the clinical situation. These high-level strategic recommendations, with various grades of evidence, can be either positive, e.g. adopt this second line of treatment, or negative, e.g. avoid prescribing antibiotics, which are not useful for this disease. The last step involves comparing the user's strategy with the system's recommendations. If the two are compatible, no alert is issued. If the user's strategy matches a negative recommendation, or if it does not match a positive recommendation, the user is alerted and the best strategy available is recommended.

The knowledge resources used for the critic mode are the ATC classification, in which upper classes are used as generalized representations of the user's prescription, accounting for treatment strategy and IF-THEN rules, which translate elementary guideline-based recommendations. Typically, the conditional part includes the reason for prescribing, e.g. hypertension, the intentional therapeutic level, and patient-specific conditions (inclusion and exclusion criteria). The action part contains strategy-level recommendations for treatment according to ATC classes with evidence grades and documentation.

Guided Mode

The guided mode aims to provide the user with a patient-centered solution to a given therapeutic problem. It is based on exhaustive modeling of a therapeutic field as a decision tree, producing a nosological inventory of all theoretical

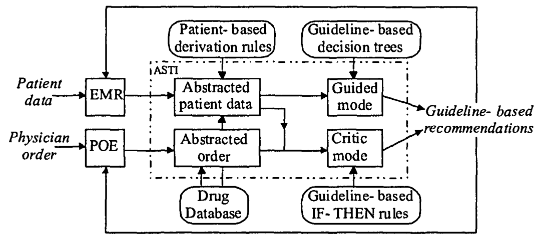

Figure1 - ASTI components and their interactions

clinical situations to which appropriate therapeutic strategies are attached. The decision tree is traversed by the physician-controlled navigation from its root to one of its leaves through the dynamic assignment of decision parameters at each node. This kind of knowledge base can be used in a non-automated way: it may be browsed by the user who interactively determines, on the basis of his interpretation of the patient's current state, the theoretical clinical profile that best corresponds to his patient in the tree. However, it can also be used in a semi-automated way: some parameters may be automatically set from the patient model and submitted to the physician for approval during the hypertextual navigation. However, more "subjective" parameters, that are contextual and require professional clinical interpretation for their determination, e.g. *Cardiac-function = good* or *poor*, must be controlled on-line by the physician. At the leaf level of the decision tree, the user obtains recommendations which he can select to plan his therapeutic strategy.

Architecture of ASTI

The ASTI system should be considered as an add-on to an existing POE system which it improves by adding extra functions. It must be connected to an EMR. In this project, we decided to use the éO electronic medical record[2], because it is the EMR used by the SFTG (« Société de Formation Thérapeutique du Généraliste »), the GP's association, which is involved as a partner in this research. éO is a problem-oriented medical record and stores free information as well as ICD-10 codes or any user-customized thesaurus. The Banque Claude Bernard[3] is the drug database associated with the éO EMR. Its contents is used for drug-centered checks and provide type-1-error criticisms of the physician's order. However, the drug database cannot provide guideline-based recommendations. Guideline knowledge is distributed within two knowledge bases, IF-THEN rules to describe elementary treatment recommendations, and decision trees to represent all the therapeutic strategies in a given medical domain. The fourth knowledge base is made out of patient data derivation rules used to built the right level of abstracted formal model for the patient state from patient data recorded in éO. Figure 1 illustrates main functional components, knowledge

[2]The éO software is a product of Silk-Informatique, France.

[3]The Banque Claude Bernard drug data base is a product of RESIP, France.

ressources, and data flow for ASTI.

A simulated case description

Consider the case of a 73-year-old diabetic patient treated for hypertension for 7 years. After one month of a treatment with a new therapeutic association of captopril and nicardipine hydrochloride, in addition to insulin, she presents edemas on the feet which appeared 3 weeks after she began to take nicardipine hydrochloride. Her blood pressure remains uncontrolled (175/75); cardiac function is normal but the patient is bradycardic, and renal function is good (clearance estimated at 60 ml/mn) with no microalbuminuria. The physician decides to modify the treatment.

Usual POE systems

Suppose that the physician enters this new prescription:

Hypertension:	captopril 50 mg tabs, twice daily
	furosemide 40 mg tabs, once daily
Diabetes:	2 injections of insulin daily (morning and evening)

Three drug-centered alerts may be issued to warn the physician to monitor the hyperglycemic effect of the captopril-insulin combination and the hypoglycemic effect of the furosemide-insulin combination as well as the synergic antihypertensive effect of combining captopril and furosemide.

ASTI in Use

Preliminary step: patient data abstraction

I10 and E10 are the ICD 10 codes for hypertension and diabetes, angiotensin converting enzyme is denoted as ACE, calcium-channel blockers as CCB, loop diuretic as LD and low dose thiazide diuretic as LD-TD. Table 1 illustrates the data derivation process that builds the patient model (ATC codes are not given here for simplicity).

Table 1. Raw and derived patient data

Raw Data	Derived data
Age = 73	Age > 60
Disease =(I10, E10)	
Cardiac-Function = good	
Cl = 60 ml/mn	Renal-Function = good
Feet-edemas = present	
Last-treatment = ((I10: captopril, nicardipine hydrochloride), (E10: Insulin))	Last-Treatment = ((I10: ACE, CCB), (E10: Insulin))

Critic mode:

Using ASTI system in the critic mode, the physician's prescription is analyzed as far as patient state, abstracted from the patient findings recorded in the EMR, and guideline knowledge represented by IF-THEN rules, are concerned.

- First step: physician prescription abstraction
  Captopril -> ACE inhibitor
  Furosemide -> LD
  Insulin -> Insulin
- Second step: search for guideline rules that apply
  If I10 and E10 and monotherapy Then ACE
  If I10 and E10 and bitherapy Then ACE and CCB
  If I10 and E10 and bitherapy Then ACE and LD-TD
- Third step: Comparison

  As most recent treatment of the patient already includes ACE and CCB, then a combination of at least two therapies has to be considered and the best candidate combination is ACE and LD-TD. After comparison of the physician's prescription and the guideline recommendation, a criticism of the physician's choice is displayed indicating that « For patients with diabetes and hypertension, the preferred therapy is the combination of an ACE inhibitor and a low-dose thiazide diuretic » which may lead the physician to modify the class of diuretic to be used.

Guided mode:

Suppose the physician finds it difficult to decide on a treatment for this patient. He may then want to use the guided mode of ASTI to get to the best patient-specific treatment recommendations. Patient data is extracted from the EMR to preinstanciate the decision tree. The navigation is then interactively carried on along the decision tree through the instanciation of patient parameters: *older than 60 years* (semi-automatic from the patient age), *diabetic* (semi-automatic from the patient history), *already treated* for hypertension (semi-automatic from patient last treatment). Then, the physician has to establish the intentional level of treatment by indicating that the patient is already treated with a combination of two antihypertensive agents. He is then proposed to acknowledge that the patient is currently being treated with the combination of an ACE inhibitor and a CCB, among other drugs (semi-automatic from patient history). When asked if CCB administration may be pursued, he answers that CCB should be stopped (due to feet edemas). Then *renal function* is semi-automatically set as *good*, leading to the final system proposition of the combination of an ACE inhibitor and a LD-TD.

Discussion

The two approches to guideline-based prescription support proposed within ASTI provide alternative and complementary methods for disseminating guideline-based knowledge in routine practice and should enhance usual POE systems.

Operating as a fully automated background process, the critic mode has the advantage of not disturbing habitual user order entering. It only warns the user when obvious strategic errors are detected. As new recommendations are published, rule-based knowledge bases can be readily updated because they are modular. However, rules embedding knowledge-based alerts must exist in the knowledge base for an alert to be issued. In addition, all the information required to trigger the rule, i.e. the condition part, should be present and correctly encoded in the EMR. However, CPGs do not cover the whole therapeutic field of a given disease and some relevant clinical situations may be omitted. These « knowledge gaps » are usually transferred to rule-based knowledge bases leading to the potential non-detection of prescription errors. Besides, the EMR is rarely comprehensive or accurate enough to rely on completely. Finally, the straightforward triggering of encoded CPG knowledge, as a result of a formalization process that is by nature context-insensitive, may yield inappropriate recommendations and criticisms. This is an important obstacle to the acceptance by physicians of knowledge-based systems dealing with complex situations.

The guided mode, initially proposed with OncoDoc [11], is in some respect, a response to the disadvantages of automated recommendation delivery. The systematic and rigorous development of a decision tree requires the "knowledge gaps" of CPGs to be filled, for instance by experts (with necessarily lower grades of evidence), which ensures the exhaustive coverage of a therapeutic problem space, i.e. the user is always provided with *a solution* for any particular situation. The interactive browsing of the knowledge base permitting contextual interpretation of the clinical situation ensures that the solution reached is *the best patient-specific solution*. By definition, the decision process is independent of uncoded or difficult-to-encode items and of unrecorded data in the EMR. However, access to the recommendations in the guided mode must be a voluntary choice of the user. As decision trees offer a globally consistent view of therapeutic strategies, both the development and maintenance of such representations require a large amount of work.

Conclusion

ASTI is a knowledge-based decision support system embedding CPGs knowledge to enhance available POE systems. We are currently developing a prototype of ASTI. Textual guidelines concerning hypertension are being encoded as rules and decision trees. A real-world evaluation handled by the GPs of the SFTG is planned.

References

[1] Evans RS, Pestotnik SL, Classen DC, Clemmer TP, Weaver LK, Orme JF Jr, Lloyd JF, Burke JP. A computer-assisted management program for antibiotics and other antiinfective agents. *N Engl J Med*, 1998: 338, pp. 232-8.

[2] Coste J and Venot A. An epidemiologic approach to drug prescribing quality assessment: a study in primary care practice in France. Med Care, 1999: 37, pp.1294-307.

[3] Teich JM, Merchia PR, Schmiz JL, Kuperman GJ, Spurr CD, Bates DW. Effects of computerized physician order entry on prescribing practices. *Arch Intern Med*, 2000: 160, pp.2741-7.

[4] Bates DW, Leape LL, Cullen DJ, Laird N, Petersen LA, Teich JM, Burdick E, Hickey M, Kleefield S, Shea B, Vander Vliet M, Seger DL Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. *JAMA,* 1998: 280, pp. 1311-6.

[5] Fox J, Johns N, Rahmanzadeh A. Disseminating medical knowledge: the PROforma approach. Artif Intell Med, 1998: 14(1,2), pp. 157–82.

[6] Ohno-Machado L, Gennari JH, Murphy SN, Jain NL, Tu SW, Oliver DE, Pattison-Gordon E, Greenes RA, Shortliffe EH, Barnett GO. The guideline interchange format: a model for representing guidelines. *J Am Med Inform Assoc*, 1998: 5, pp. 357-72.

[7] Musen M, Tu S, Das A, Shahar Y. EON: A component-based approach to automation of protocol-directed therapy. *J Am Med Inform Assoc*, 1996: 3, pp. 367-388.

[8] Shahar Y, Miksch S, Johnson P. The Asgaard project: a task-specific framework for the application and critiquing of time-oriented guidelines. Artif Intell Med, 1998: 14(1,2), pp. 29–52.

[9] Purves IN, Sugden B, Booth N, Sowerby M. The PRODIGY project - the iterative development of the release one model. J Am Med Inform Assoc, 1999: 6(suppl), pp. 359–63.

[10]Johnson PD, Tu S, Booth N, Sugden B, Purves IN. Using scenarios in chronic disease mqnqgement guidelines for primary care. J Am Med Inform Assoc, 2000: 7(suppl), pp. 389–93.

[11]Bouaud J, Séroussi B, Antoine EC, Gozy M, Khayat D, Boisvieux JF. Hypertextual navigation operationalizing generic clinical practice guidelines for patient-specific therapeutic decisions. J Am Med Inform Assoc, 1998: 5(suppl), pp. 488–92.

[12]Sowa JF. Conceptual structures: information processing in mind and machine. Addison-Wesley, London, 1984.

[13]Feldman RD, *et al.* 1999 Canadian recommendations for the management of hypertension. Can Med Assoc J, 1999: 161, pp. SF1-SF25.

Address for correspondence

Dr. Brigitte Séroussi
Service d'Informatique Médicale
91, boulevard de l'Hôpital
75634 Paris cedex 13
France
bs@biomath.jussieu.fr