POLISH ACADEMY OF SCIENCES
Systems Research Institute

# APPLICATIONS OF INFORMATICS IN ENVIRONMENT ENGINEERING AND MEDICINE

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# CHAPTER 3

## Informatics and Economy in Environment and Health Protection

# FROM PAPER BASED TO ELECTRONIC GUIDELINE: AN INTERNET BASED DECISION SUPPORT SYSTEM IN MEDICAL PRACTICE

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*In order to develop an internet-based decision support system, making available for French general practitioners several prevention guidelines is was necessary to implement paper based guideline. We propose a framework allowing to transform paper based practice guideline into their electronic form. Three different problems were identified: computability (e.g. determinism of the eCPG), logic (e.g. ambiguities when combining Booleans operators) and external validity (i.e. stability of decision for variations around thresholds and proportion of subjects classified in the various terminal nodes).The last problem concerned documentation of evidence: the level of evidence was associated only with the terminal decision node and not with the pathway through the decision tree. We concluded that computerization of guidelines is not possible without expertise or authors advices. To improve computability it is necessary to provide authors with a framework that checks ambiguities, and logical errors*

**Keywords:** Practice Guideline, algorithm, software.

## 1. Introduction

Since the 90's, the number of clinical practice guidelines (CPGs) has dramatically increased (Hibble, 1998). These CPGs are developed by official Agencies, such as the Agency for Healthcare Research and Quality (AHRQ, 2005) in the United States or "Agence Nationale pour l'Accréditation et l'Evaluation en Santé" (ANAES, 2005) in France and by Academic Societies. However, CPGs are scarcely put into practice by end-users, namely general practitioners. Little evidence of their effectiveness to improve medical practices is currently available. One way to get valid knowledge at the point of care, is to make guidelines available under a synthesized format. Moreover, taking into account the complex knowledge used in guidelines (associating quantified results and level of evidence, risk equations and/or decision trees) help decision making with computerized tools. This paper reports the strategy of guidelines implementation in the EsPeR project (Individualized Estimate of Risks), the framework used and the different problems encountered. This project provides doctors with appropriate risk estimates and corresponding CPGs, individualized according to individual patients characteristics.

## 2. Materials and methods

The decision support system (DSS) of the *EsPeR* Project consists of the two parts of prevention: evaluation of risks and computerized guidelines. The DSS is based on CPGs implementation using appropriate elements of electronic patient record. The CPGs written by academic societies or official Agencies according to an explicit methodology, provide an initial material to constitute the knowledge base of the DSS. We selected two cardiovascular CPGs dealing with the management of adults with essential hypertension (1997 for the first version and 2000 for the second version), and the 2000 hypercholesterolemia guideline, all issued by the ANAES. Simple rules described by the Evidence Based Medicine Working Group make it possible to identify the valid and useful CPGs in practice (Guyatt, 1995). In agreement with the educational objective pursued by the *EsPeR* system, two types of knowledge are provided in the DSS. The first type consists of the content of a CPG, and the second type consists of the support for its level of evidence.

*Theoretical framework*

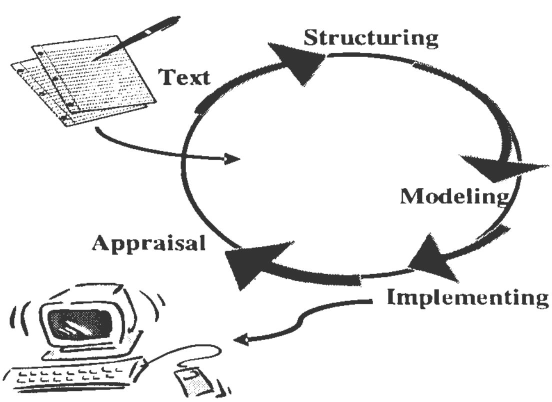


**Figure 1.** *eCPG life cycle*

To transform the CPGs into an electronic DSS format, we developed a framework with different steps that we call "the life cycle" (Figure 1).

### 2.1 Structuring

The first step consist in structuring the textual CPG. To do this, several ways can be followed (Lobach, 2000; Bernstam, 2000). We chose first to transform the text into a linear algorithm. The successive steps are the following: 1) extraction of relevant information, 2) tree specification: nodes (i.e. conditions "age < 60 years old"), branches (results of the conditions), messages associated to terminal nodes. Building the tree from the text-based guideline is mainly human.

## 2.2 Modelling

The role of the modelling step is to fit the structured CPG within a given knowledge representation model. Several models of the structured knowledge representation have been described for the CPGs in the literature. The GuideLine Interchange Format (GLIF) model (second version) has been selected and adapted in *EsPeR* because its structure appropriately fits our requirements (Ohno-Machado, 1998):

- Representation of a starting point in the CPG,
- Representation of an action (by a single entity), representation of some option following this action and some criteria for its execution,
- Representation of a complex CPG (sequence of several conditions and actions),
- Representation of clinical data linked to patient record,
- Representation of links on information sources entailing documenting the level of evidence.

## 2.3 Implementing

Each CPG is implemented as one independent unit which takes as input the clinical data of a given subject and outputs a screening or therapeutic advice targeted to this subject. Its execution relies on the association of a model of knowledge representation and an inference engine. For implementation, we selected the Java Language because of its multi-platform deployment capacities. A specific Java applet was built for each *eCPG* Some classes are used by several domain *eCPG* like the I/O class but other are specific.

## 2.4 Appraisal

Critical appraisal should be a continuous process throughout the development of an *eCPG*. The concepts of internal validity and external validity can be used to assess the *eCPG*. Internal validity addresses the computability and the logical aspect of the guideline and external validity its value for the end-user and its consequences if applied appropriately in the population. We defined 3 groups of indexes to estimate validity. The first two groups include indexes related to internal validity: computability, and logical properties.

*Computability properties*

- determinism of the *eCPG* (all the sample get a message),

- distribution of messages,
- number of different messages for the same case,

*Logical properties*

- ambiguities when combining Boolean operators,
- order effect (the results varies depending on whether the order of the two conditions constituent of a complex node),
- hierarchical effect. For example to classify a sample in one of three classes with two thresholds, one of the threshold has to be tested first usually the lowest or the highest. The order of the test could influence the distribution output.

*External validity*

The third group of indexes deals with the clinical value of the guideline, particularly: stability of decision for variations around thresholds (arbitrary choice of threshold, lack of precision of measurements), and proportion of subjects classified in the various terminal nodes. This requires the use of epidemiological data, or testing the CPG in the real world. For this purpose, we used a dataset of 15 444 hypertensive subjects included in the place groups of various hypertension trials of the treatment of mild hypertension (INDANA database) (Gueyffier, 1995). Using this database, we simulated the response of the guideline for varying values of some critical decision nodes. The appraisal step feed back to the CPG authors all the results of the indicators defined above.

### 2.5 Level of evidence

Nowadays, validity of a knowledge must be appraised according to principles of Evidence Based Medicine (Evidence-Based Medicine Working Group, 1992). The level of evidence applies to any kind of knowledge: statistical models or clinical prediction rules must meet clearly defined quality criteria (Laupacis, 1997); similarly, knowledge-based decision algorithms must implement the most up-to-date and valid knowledge. Within the framework of this project, we used only CPGs developed according to an explicit method (Hayward, 1995). However, within an algorithm, there are several different ways for reaching the same terminal nodes. Each of this path should therefore have its own level of evidence. This point is not addressed in this paper. We only used the level of evidence associated to each terminal node as it was provided by CPG authors.

## 3. Results

The CPG for the diagnosis and the management of hypertension was first implemented in the system. The input variable are the Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), age, cardiovascular (CV) history, CV risk factors and the temporal confirmation of the blood pressure measure. The CPG provided two final messages: treatment and no treatment.

### 3.1 Internal validity

*Computability*

At the end of implementation, each input sample in the computerized tool provide one and only one message output. Under the hypothesis of equi-probability of each values of the input variables and some limits for the quantitative data as SBP and DBP, the distribution of different messages was checked.

*Logic*

We identified several problems during implementation. The first step of the CPG is a combination of Boolean operators written "SBP > 140 mmHg and/or DBP > 90 mmHg". This test message doesn't explain which one of the DPB or SBP should be considered first and whether the operator "OR" prevails against the operator "AND" or the contrary. For the strict OR option the order effect appears. For example, if we use the SBP selection first, every measure of SBP higher than the 140 mmHg is enough to go to the next step without taking into account any DBP value. And this DBP value could be higher than the higher threshold. So we point here a possible underestimation of measured blood pressure couple.

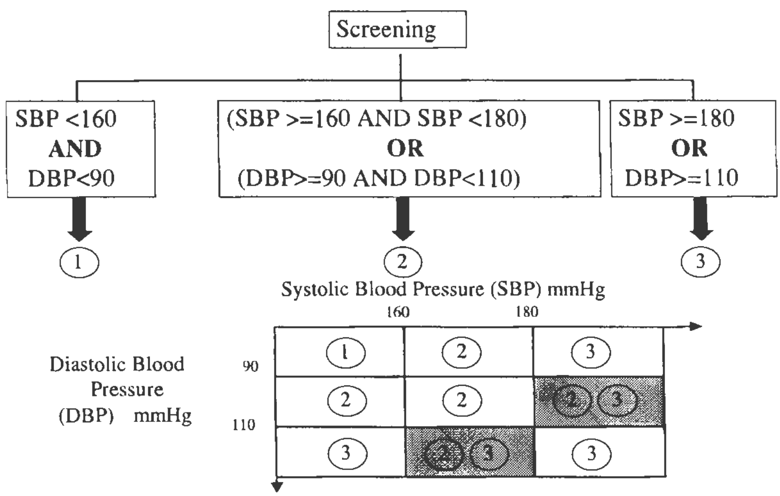


**Figure 2.** *Hierarchical Effects*

For the three branch condition step (figure 2), the text of the three boxes concerning the SPB and the DBP, information about the interpretation of Boolean operators is needed. We identified two main problems: the Boolean operators definition and the hierarchical effect. Concerning Boolean operators, the two boxes having the highest threshold, the operator of the guideline is "AND/OR", and for the third the lowest is "AND". If we use this selection and interpret AND/OR as a logical OR, we face a choice problem as shown in the figure 2. We point out for two cells a choice problem between 2 and 3 (figure 2). These cells are available through the highest two threshold boxes. A choice is needed

All the problems listed below were found in the first version of the hypertension CPG. The Boolean and hierarchical effect was also found in the second version.

### 3.2 External validity

An example of simulation on real data is shown on figure 3. We use the question "is there a confirmation of the blood pressure level over several visits?", since repetition of blood pressure measurements is an important (and often missing) element of hypertension management.

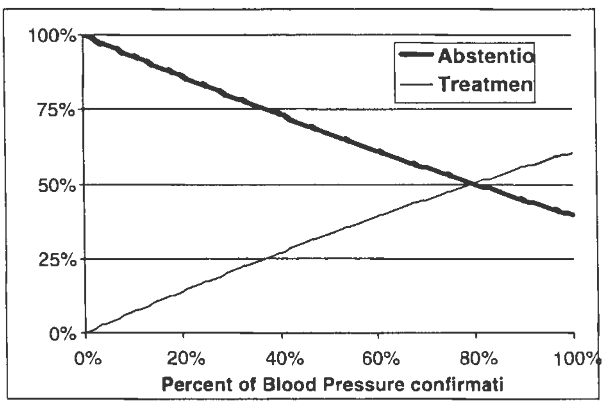


**Figure 3**. Effect of blood pressure confirmation on the proportion of messages

If the answer is "no" for all patients, the guideline give always the same message: "do not treat". When the proportion of "yes" increases, the proportion of patients for whom the system recommends treatment increases to 60% with an equilibrium between the 2 types of messages reached when confirmation occurs in 80% of the patients.

### 3.3 Hypertension *eCPG* interface

A decision tree in the interface of the CPG unit represents the algorithm of the guideline. This decision tree is built dynamically in the left panel to help the users understand the reasoning process (figure 4). In this tree, each part of the model is represented with a specific graphic code: action steps (i.e. queries on patient data) in light grey boxes (1), condition steps (i.e. tests on retrieved patient data)(2), and the final step (i.e. appropriate medical advice) in a dark box (3).

- in the right panel, three other fields display the following information:
  - a recall of variables taken into account for this advice,
  - a text field (4) provides definitions for the current query on patient data (for example: "was the blood pressure level confirmed over three different consultations?")
  - a text field (5) for the recommendation message and its corresponding grade
- the "Grades" button gives access to generic definitions of the levels of evidence according to the Oxford Center of Evidence Based Medicine (http://www.oxforfd.uk.cebm).
- the "More about..." button gives access to explanations of the grade specified in the current recommendation message.

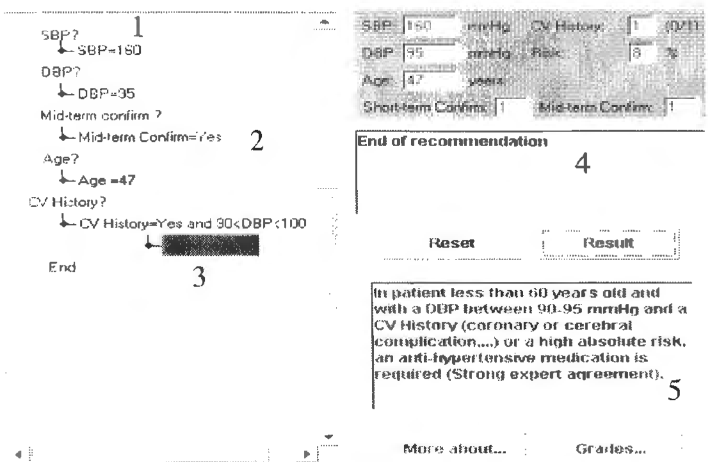


**Figure 4.** Interface of the first hypertension guideline

## 4. Discussion

Today, the publication of CPGs by health agencies fails to impact the effectiveness and efficiency of care. This observation has at least two explanations: inflation of CPGs (Hibble, 1998), and their lack of availability at the point of care in a format that can actually help the decision making process. Indeed, only DSS based on active alerts or reminders may modify clinical practice (Shea, 1996).

Recommendations are currently available on the Internet, but the time necessary to the exploitation of their content is not compatible with the average duration of a visit. Their modelling and integration within an electronic record is the solution chosen in the *EsPeR* project. However, we show in this paper that many difficulties were encountered for implementing text-based guidelines.

**Knowledge content**

Textual data in CPGs requires a degree of interpretation, which induces a risk of variability at the level of the message content. Indeed recommendations sometimes reveal ambiguities, inconsistencies or lack of fulfilment in their drafting which make them not always decidable. Structuring and modelling according to the GLIF model makes it possible to highlight these problems and to require an expert's intervention to correct their imperfections.

As an example, it is written in the French hypertension CPG: "For patients aged between 60 to 80, with sole systolic hypertension, the aim is to reduce systolic BP to 160 mm Hg or less, regardless of the diastolic BP (strong expert consensus). Elderly patients should be screened for orthostatic hypotension, and the doctor should aim to progressively lower blood pressure using lower doses of medication than those used for younger patients." (ANAES, 2005). How to interpret in this text "orthostatic hypotension ", to represent "a progressive lowering of blood pressure" and to grade the level of evidence "strong professional consensus"?

Currently, practice guidelines remain imperfect as regards the way knowledge is presented. Efforts should be made in order to avoid ambiguities, which may need expert support for computerization.

**Framework**

The quality management of the implementation based on different criteria (internal and external validity) provide us from scratch with a functional DSS. The internal validity gave us the opportunity to optimise the paper source interpretation, by asking for the author's precisions when it was necessary. Without any expertise or information from the authors of the CPG, the guideline cannot be implemented. The Boolean operator's effect and the hierarchical effect are still in the CPG.

To cancel the hierarchical effect, the authors of the first version, propose considering the higher threshold selection first. Thus the algorithm checks all blood pressure couples from the highest to the lowest thresholds. A patient with 170/120 BP and another with 170/100, will not take the same way in the decision tree with this solution. This effect is the consequence of a combination of two variables in the same level of choice. Another solution should be to dissociate in time, the selection for the SBP and the DBP. Nevertheless, all these optimisations and corrections are time consuming by the need to contact the CPG authors.

**Evidence documentation**

To associate to decision, a level of evidence is an important objective of the *EsPeR* system. Gathering the level of every piece of knowledge used in the *EsPeR* system was a complex task, either because existing evidence is not always clearly reported in CPGs or simply because relevant evidence is not available for all the possible clinical scenarii. However, it is important to document any recommendation by a level of evidence without stopping the decision-making process when the evidence does not exist (Feinstein, 1997). In this case, intervention of one or several experts is necessary and must be explicit (grade D recommendation).

Moreover, information to document level of evidence can be complex enough to be structured by a generic model. A solution has been proposed in the literature (Shankar, 1999). In the *EsPeR* system, this information is presented by dynamic HTML pages, and should evolve towards a more structured model.

**Other Limits**

All these difficulties underline the limits of CPGs and *eCPGs* as a formal framework to represent knowledge. Other approaches for knowledge representation or even knowledge acquisition (i.e. case based reasoning, symbolic machine learning.) would be perhaps interesting. In the present state of development of our project, we identified three different ways for improving both guideline computability and efficiency. The first would be to use a framework of guideline development for developing guideline, to avoid errors discussed above at the beginning of the development process.

The second concerns shared knowledge. By implementing different CPG within the same domain (hypertension and cholesterol) we found that the different *eCPGs* were not independent. They use frequently the same concept as cardiovascular risk factors. Some "sub-guidelines" should be shared between different *eCPGs*. Within the cholesterol *eCPG*, hypertension is included as a cardiovascular risk factor and can interact with the cholesterol management process. The same interaction is found in the hypertension CPG with the concept of elevated values of cholesterol. Since many diseases are not independent from each other, *eCPG* developers should better define shared domains and concepts. Presently, in the absence of such a strategy, the creation of a cardiovascular meta-CPG is another limiting factor in the development of computerized guidelines.

The decision tree assumes that queries provide true answers. In many situations, for a given node, it is not possible to give any binary answer to a question. However, a tree that allows answering with a partial yes or no would have a much larger number of terminal nodes. In real world problems, the intuition of a human expert, or expert system software, is necessary to determine the likely terminal node. Fuzzy logic is an approach for dealing with uncertainty (Jaulent, 2001). For each node and branch, a value is associated and propagate through the tree, until the terminal node. On a given branch, the value expresses, to which extend the choice of this branch is valid according to previous node. And at the levels of the terminal nodes the final value expresses to which extend the message is true for this specific patient. Such an approach could be included in the next package.

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**(Editors)**

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The purpose of the present publication is to popularize applications of informatics in environment and health engineering and protection. Runned papers are thematically chosen from the works presented during the conference *Multiaccessible Computer Systems* (*Komputerowe Systemy Wielodostępne*) that has been organized by the Systems Research Institute and University of Technology and Agriculture of Bydgoszcz for several years in Ciechocinek. Problems described in the papers concern quality management of the surface waters and the atmosphere, application of the mathematical modelling in environmental engineering, and development of computer systems in health and environmental protection. In several papers results of the research projects financed by the Polish Ministry of Science and Information Society Technologies are presented.

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