M. Fieschi, J. Gouvernet

Laboratoire d'Enseignement et de
Recherche sur le Traitement de
l'Information Médicale,
Faculté de Médecine de Marseille,
Marseille, France

Commentary

Reasoning Foundations of Medical Diagnosis Revisited

Reflections on R.S. Ledley's paper:
Reasoning Foundations of Medical Diagnosis

In Butterworth's Medical Dictionary (1965) diagnosis is defined as the art of applying scientific methods to the elucidation of the problems presented by a sick patient. Thus, it made sense to try and incorporate mathematical methods that would be likely to enrich this art. As soon as computers were available to physicians, the question of arriving at a diagnosis using automatic methods became a major research topic.

Naturally, while automatic methods would not provide a tool to replace the physician, they were nevertheless useful in several respects in analyzing how a diagnosis was reached along with the mathematical and statistical tools proposed to formalize the problem.

The aim of this pioneering research was usually to arrive at a correct diagnosis by being able to incorporate all the information contained in the medical record. The technology of the period had something to do with this approach. It must be remembered that only batch processing was possible at the time, and the interactivity required to design a step-by-step decision-support tool, and that the best strategy was out of reach. We will come back to this point later on.

Among all the articles that appeared before 1960, the article by Ledley and Lusted [1] is the most important in our view. It presents in perfectly clear terms the problem of diagnostic decision making and, from a methodological standpoint, the broad lines of the paths it laid out for research are worthy of interest even today. Re-reading it at a distance of almost 40 years allows us to assess the influence of the concepts it introduced on the development of medical information technology as well as those that are still presently used. It also enables us to analyze the causes of the labile nature of other proposed concepts or approaches. Re-reading these seminal articles is, in fact, a research approach.

The Analysis Model Proposed by Ledley and Lusted

Before looking into the notions introduced in the article, attention should be drawn to its pedagogical quality, an essential quality in 1959, since few clinicians were familiar with symbolic logic, probability theory and mathematical expectancy. For most of them, a computer was a rare machine, dedicated to more or less mysterious numerical calculations in no way intended to help them solve their everyday problems.

The first, introductory part of the article is surprisingly up-to-date. The problem was formulated 40 years ago and we still pose it today in often similar terms:

- The possible use of computers as an *aide-mémoire*, both for gathering relevant information and calling up a diagnosis, remains the stated aim of researchers in the field today.
- The pedagogical contribution to the student, learning differential diagnosis, is already present and announced as a benefit to be found in the use of computers.

The authors underscore the need for an analytical approach to achieve a grasp of diagnostic reasoning. They characterize it by the use of three basic concepts inherent in every diagnosis: (1) symbolic logic, (2) probability theory and (3) utility theory, the latter being useful in therapeutic decision-making.

The combination of these modes of reasoning was taken up again later on by other authors who sometimes assigned them different roles in the decision-making process. We might mention, in particular, Szolovits and Pauker who, in another important article [2], took up the idea 20 years later, insisting on the fact that any system shown to be genuinely capable of expertise in the medical field had to use "a judicious combination of categorical and probabilistic reasoning". The first was necessary to set the limits of the decision-making context, and the second to make comparisons between the hypotheses considered and possibly to propose a therapy.

Numerous other authors turned towards the methods of decision-making analysis introduced in the article. These methods propose an explicit, logical framework to create a model of decision-making situations [3,4].

The first essential notion presented in the article is the breakdown of the diagnostic approach into three steps, which are as follows:

- determine possible diagnoses,
- attempt to order the various possibilities,
- choose the most useful actions.

The first step is aimed at selecting possible diagnoses. To carry out this selection, the authors propose to use symbolic logic and the model $E \rightarrow (G \rightarrow f)$ in which E represents knowledge, G observation, and f the diagnosis. The solution then involves finding the Boolean function that satisfies the above-mentioned formula.

In this logical stage, the knowledge used represents logical or categorical links between diagnoses and symptoms. This formulation has two important implications:

- the knowledge used must be completely independent of any observation,
- the symptoms are considered simultaneously and not in sequence.

The authors emphasize that most errors are due to the omission of diagnoses that should be taken into account. In order to limit errors, knowledge E must be exhaustive.

The symptoms and diagnoses are binary, E is a Boolean function of the `Diagnoses*Symptoms` set produced.

The second step involves trying to order the various elements selected, more specifically assigning a probability to each one. This is done using Bayes' formula which allows the calculation of P(f/G) starting from the probabilities P(G/f) (i.e., the probability of patients with a particular illness presenting one or more symptoms). The authors point out that this latter expression corresponds to the knowledge contained in medical textbooks.

- Conditional probabilities P(f/G) are the expression of medical knowledge, their values are therefore stable, they are valid for all practitioners.
- A priori probabilities are linked to recruitment, time of recruitment, geographical location, seasonal influences, etc. They must be estimated for each practitioner and, if necessary, constantly updated.

The third step involves choosing the appropriate action. The action selected as optimum is the one which maximizes the expected utility.

If the physician has not succeeded in assigning probabilities to the various possible resulting situations, the authors propose adopting a mixed strategy and using theMaximin principle.

In addition to the general model presented above, the article suggests a method for estimating probabilities using as a base the cases of patients for whom the diagnosis is already known. This method made it possible to further the estimation of probabilities and prefigured learning research which was to be developed later on.

The authors opened the way to research and thinking on how to formalize diagnostic reasoning. The methods presented as well as the paradigm of their use have been widely disseminated and have served as a standard for research in medical informatics. The logical phase has been used in computer-assisted diagnosis making by many researchers. Assigning probabilities to diagnoses, particularly using Bayes' formula, has given rise to a large number of applications. Among these, we should mention the very important contribution of De Dombal and his team [5]. Finally, the principle of maximizing expected utility and its use, especially in decision trees, has provided the basis for numerous systems.

Initial Considerations

The breakdown into three steps is still valid today, whether it is explicitly stated or we are placed from the outset in the situation belonging to one of the phases. The limits of the approach with regard to diagnostic problems concern several points of varying importance:

1. Refinements and improvements are, of course, needed to take the reality of the situation more fully into consideration:
   -Taking into account non-binary symptoms. To process continuous or discrete quantitative data, the ranges of values for normality and standard intervals must be determined. Everyone is familiar with the complexity of this problem and the limits of this mode of representation.
   -Data, even when they are processed in a Boolean fashion, may themselves be uncertain. Introducing a certainty factor into the description of data has been the subject of a great deal of research for over 20 years. Fuzzy set theory [6], for example, has given rise to a number of applications aimed at enriching the Boolean model, which is often oversimplified.
   - Joint modeling of logical rules and probabilities [2] to describe the diagnostic process.
2. The model is easily applicable in the ideal situation in which the patient has only one illness. However, reality is often more complex and adapting the model to cope with disease combinations then becomes problematic.
3. In the article by Ledley and Lusted, observation is supposed to be achieved in one step, or at least, without any further steps required. This means that the approach enabling the acquisition of the information required to make the diagnosis is not mentioned.

Table 1. Diagnostic methods adapted from Deutsch et al. [10].

Medical knowledge	Inference engine	Remarks
Clinical cases	Classification tree	Follow instructions in an algorithm
Clinical cases	Pattern recognition	Find a similar patient in the database
Neural net	Pattern recognition	
P(D), P(f/D), risks and utilities	Bayes and decision theory	Rank-order hypotheses
Discriminant function	Discriminant analysis	Compute a posteriori probability of diseases based on discriminant function
Belief measures	Demster Shafer theory	Compute degree of belief in single and combined disorders
Production rules	Rule-based inferencing	Infer diseases with certainty factors or possibility measures
Criteria table	Criteria–based reasoning	Match findings to disease descriptions
Causal model of diseases	Model-based reasoning	Pathophysiological pathways from etiologies to findings

In our opinion, this last point is the most important one, because the use of reasoning, which tends to restrict the boundaries of the search for diagnostic hypotheses to be considered, is not apparent. It is very significant, however, in the field of diagnosis; it involves heuristic reasoning that has given rise to a good deal of research in artificial intelligence [7].

What is Learned and Further Considerations

The limitations of the Ledley and Lusted model have resulted in their being profoundly called into question. It is impossible to mention here all the significant contributions that have been proposed. An attempt was made to propose sequential use of Bayes' rule after every observation of a symptom or to use Bayes' rule when the observed symptom is uncertain (the user can then qualify the symptom in terms of its degree of certainty). An attempt was made to evaluate the impact of hypotheses regarding the interdependence of symptoms and the interdependence of diagnostic hypotheses. Reasoning under uncertainty has been the subject of other attempts to offset the constraints of probability theory. For example, Carnap's inductive logical theory [8] introduces a function *C*(H/E) which represents the degree of confirmation of an hypothesis H, given evidence E. It has been proposed to help define rational decision making.

From this thinking, systems arose that are based on various scoring functions allowing the hypotheses present to be organized into a hierarchy. This is the case, for example, of the PIP system [9]. A further idea has developed regarding the role of scoring: it must serve as a basis for more complex symbolic strategies. Numerous other approaches have also been proposed to offset the difficulties encountered; they are presented in outline form in Table 1, adapted from [10].

As a general rule, this research tends to solve a classification problem consisting of deciding to which predefined subset of objects a particular object belongs. Given the complexity that may exist in reality, this model is sometimes found to be at fault. Some authors have approached the problem differently, by developing a sequential diagnostic model and using causal knowledge of physiopathology that explains the patient's symptoms. Building a "patient-specific model" in ABEL [11] fits in with this line of research.

After the abundant literature on normative decision analysis centered on Bayes' rule, the AI approach in the years 1975-1985 left aside in large part the proposed formalism and quantification in favor of a symbolic approach.

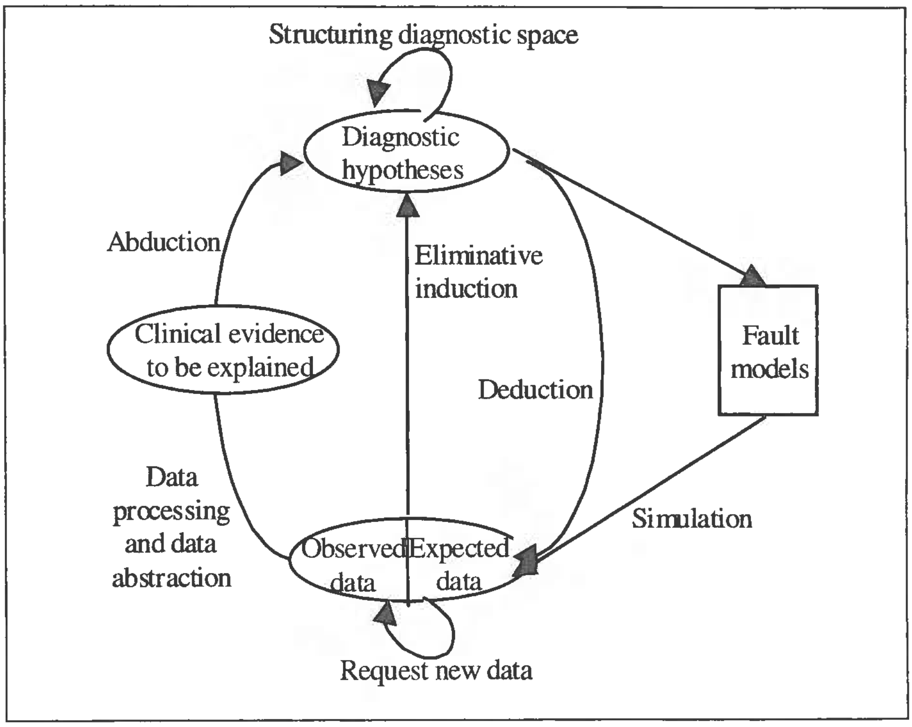
The contribution of cognitive psychology has also supplemented and diversified the models. "A human being is a selective, stepwise information processing system with limited capacity" [12]. Thus, diagnosis was identified as a dynamic cognitive process, characterized by the search for evidence to test a given hypothesis where heuristic thinking plays a significant role. This process is itself a combination of processes that are at once multiple and sequential.

The acceptability of such systems has been studied. What emerges is that it is not only linked to the program's level of expertise.

The role of differential diagnosis in structuring clinical decision-making [13] and in the physician's behavior has been reviewed and studied. This research has accompanied the development of expert systems. The approach has provided tools to help in building decision-support systems using models and knowledge, produced by software engineering resulting from this research. MYCIN was the starting point of abundant research using production rules [14,15], CASNET used a causal network of pathological states [16], PIP was already cited [9], SPHINX [17], etc. The models proposed to represent the diagnostic process were refined and made more complex, as shown in the diagram (Fig. 1), proposed by Ironi et al. [18].

While for years the debate has focused on the type of reasoning to be used in diagnostic systems, today it is obvious to many researchers that both styles of reasoning (categorical and probabilistic) must be used in an adequate way and co-exist in all intelligent systems [19].

Figure 1. A model of diagnostic reasoning adapted from Ironi et al. [18].



Conclusion

Ledley and Lusted's article deserves credit for helping to introduce the study of decision-support models into medicine. This research has developed considerably and has benefited from interdisciplinary contributions, including cognitive psychology and artificial intelligence.

Those who disparage these approaches customarily say that computer-assisted decision methods do not stand the test of medical practice in its actual day-to-day complexity. It is true that in the field of medical decision support, if we confine ourselves to listing the systems used in practice, the results would be poor. Such an assessment would also be limited. We should not forget other contributions derived from research in decision support which have taken various forms: the rationalization of medical treatment, the search for optimum strategies in the sense of well-defined criteria, quality health care at the lowest possible cost, cognitive support in medical practice (reminders, guidelines, etc.), the position and role of the expert (evidence-based medicine), and so on.

Despite quite decent performance levels, the acceptability of such systems in current practice remains an important question. It can be analyzed from two points of view:

- The interpretation and use of numeric data and probabilities to give weight to advice poses cognitive problems for ordinary physicians [20].
- Until recently designed as consulting systems, they have to be integrated into information systems corresponding to the actual exercise of medical practice.

This research has indirectly led to questions pertaining to the knowledge used by experts and the confidence that should be placed in it. In this sense, it has helped call into question the role of experts in the field of the decision-making process and the birth of the paradigm of evidence-based medicine.

Using these methods makes it easier to understand and to achieve a better grasp of the decision-making conflicts facing clinicians. It may allow us to clarify the medical debate, by bringing to the fore disagreements or decision-making biases.

References

1. Ledley RS, Lusted LB. Reasoning foundations of medical diagnosis. *Science* 1959;130:9-21.
2. Szolovits P, Pauker SG. Categorical and probabilistic reasoning in medical diagnosis. Artifl Intell 1978;11:115-44.
3. Pauker SG, Kassirer JP. Therapeuticdecision making: A cost-benefit analysis. N Engl J Med 1975;293:229-34.
4. Weinstein MC, Fineberg HV. *Clinical Decision Analysis*. Philadelphia: WB Saunders, 1980.
5. De Dombal FT, Leaper DJ, Staniland JR, McCann AP, Horrocks JC. Computer-aided diagnosis of abdominal pain. Brit Med J 1972;2:9-13.
6. Zadeh LA. Fuzzy sets. Inform Control 1965;8:338-53.
7. Pearl J. *Heuristics: Intelligent Search Strategies for Computer Problem Solving*. Reading, MA: Addison-Wesley Pub, 1985.
8. Carnap R. Inductive logic and rational decisions. In: Carnap R, Jeffrey RC, eds. *Studies in Inductive Logic and Probability*. Berkeley: University California Press, 1971: 5-31.
9. Pauker SG, Szolovits P. Analyzing and simulating taking the history of the present illness: context formation. In: . Schneider W, Sagwall-hein S), eds *Computational Linguistics in Medicine*. Amsterdam: North-Holland, 1977: 109-118.
10. Deutsch T, Carson E, Ludwig E. *Dealing with Medical Knowledge: Computers in Clinical Decision Making*. New York: Plenum Press, 1994.

11. Patil RS, Szolovits P, Schwartz WB. Modeling knowledge of the patient in acide-base and electrolyte disorders. In: Szolovits P, ed. *Artificial Intelligence in Medicine.* Colorado: Westview, 1982:191-226.
12. Hogarth RB. Cognitive processes and the assessment of subjective probability distributions. J Am Stat Assoc 1975;70:271-94.
13. Pople HA Jr. heuristic methods for imposing structure on ill-structured problems: The structuring of medical diagnostics. In: Szolovits P, ed. *Artificial Intelligence in Medicine.* Colorado: Westview, 1982:119-90.
14. Shortliffe EH, Buchanan BG. A model of inexact reasoning in medicine. Math Biosci 1975;23:351-79.
15. Shortliffe EH. *Computer Based Medical Consultation: MYCIN.* New York: Elsevier, 1976.
16. Kulikowski CA, Weiss SM. Representation of expert knowledge for consultation: the CASNET and EXPERT projects. In: Szolovits P, ed. *Artificial Intelligence in Medicine.* Colorado: Westview, 1982: 21-55.
17. Fieschi M *Artificial Intelligence in Medicine: Expert Systems.* London: Chapman and Hall, 1990.
18. Ironi I, Stefanelli M, Lanzola G. Qualitative models in medical diagnosis. Artif Intell Med 1990;2:85-101.
19. Holtzman S. *Intelligent Decision Systems.* Reading, MA: Addison-Wesley Pub, 1989.
20. Tversky A, Kahneman D. Judgment under uncertainty: Heuristics and biases. Science 1974;185:1124-31.

Address of the authors:
Marius Fieschi, Joanny Gouvernet,
Laboratoire d'Enseignement et de Recherche sur le Traitement de l'Information Médicale,
Faculté de Médecine de Marseille,
Bd Jean Moulin,
F-13385 Marseille Cedex 5,
France.
E-mail: mfieschi@aphm1.ap-hm.fr