Diagnostic Games:
from Adequate Formalization of Clinical Experience to Structure Discovery

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Abstract. A method of obtaining well-founded and reproducible results in clinical decision making is presented. It is based on "diagnostic games", a procedure of elicitation and formalization of experts' knowledge and experience. The use of this procedure allows formulating decision rules in the terms of an adequate language, that are both unambiguous and clinically clear.

Key words: clinical decision making, formalization, diagnostic games, experts' knowledge

Introduction. Evidence-based medicine and clinical experience evidence

Evidence-based medicine (EBM) and computational Machine Learning (ML) approaches became very popular in the attempt to bring a scientific support to the practice of clinical medicine. Their role is considerable and undeniable. However, an important gap exists between empirical evidence and clinical practice because evidence resulting from randomized controlled study or from computational models is not directly applicable to individual patients.

Considering a typical example of a ranking system of evidence we find something like following: "The first level: Evidence obtained from at least one properly designed randomized controlled study <...> The last level: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees".

In this hierarchy, empirical evidence obtained from a randomized controlled study is listed first. Consequently, this "evidence" viewed as the "best" on which to make a clinical decision and supersedes clinical experience that has a lowest rank in this list. As noted by M.R.Tonelli [1], clinical experience "differs in kind, not degree, from empirical evidence and does not belong on a graded hierarchy". In accordance with this he suggests to view this kind of medical knowledge as complementary to empirical evidence. He concludes that its incorporation in EBM is "necessary to overcome the intrinsic gap noted above." But it seems clear that clinical experience or a specialist's opinion by itself is not yet what should be considered as evidence. So, what we need is

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a formalization method that could produce a radically different type of medical evidence, namely, *evidence from clinical experience*.

Formalization of clinical experience is a sophisticated task because two antagonistic criteria must be satisfied: to formalize clinical concepts and features, and at the same time remain faithful to its deep insights and common sense. We call such formalization “adequate formalization”. Adequate formalization is decisive for the success of further mathematical processing and is the basis for the later stages of the work. In this paper we introduce an original experimental method aiming for adequate formalization of clinical experience. This method yields verifiable and reproducible results. The purpose of this paper is methodological; we will show the way to formulate and solve problems of clinical decision-making so that the results can be directly applicable to individual patients. The present approach was first developed in the collaborative works of Israel M.Gelfand and colleagues with clinicians in 1970s [2]. In this article we pursue this line of work.

1. Problems to solve

Problems we are tackling here constitute the essential part of patient oriented decision-making problems that emerge during the course of patients' treatment. Here are the typical examples of problems focusing on individual patients.

- "What is the diagnosis for the given patient?"
- "Is the drug effective for the given patient's outcome?"
- "What would the preferred treatment for the given patient be?"
- "What is the prognosis for the course of the disease for the given patient?"

All these problems are tied to clinical investigations with the aim of improving the treatment's results for a particular group of patients and of indicating ways to achieve this aim.

The analysis and formalization of a decision-making problem in a given clinical setting typically will lead to another patient-oriented problem which we will consider as a formal decision problem of the study. We want to stress the importance of the relation path:

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aim of clinical investigation → medical decision-making problem → formal decision problem of the study.
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We emphasize that clinically meaningful evaluation of results of the study should include the evaluation of improvement in the treatment in precise clinical settings. This means that the evaluation of the result should depend on to what degree the *aim of clinical* investigation has been achieved.

2. Clinical experience versus medical knowledge

Our formalization method for patient oriented clinical-decision problems extensively uses the *Diagnostic games (DG)* technique [3] and statistical analysis.

Statistical methods can be applied to a group of patients. Used alone they are often not sufficient for patient-oriented clinical problem [e.g.4]. The reasons for this are the following.

- Results obtained in terms of mathematical statistics need to be interpreted in clinical terms that may not always be obvious and unambiguous. For example,
if a reliable calculation of probability of success of a surgery intervention is not close to 1 or to 0, then it is of little use for a doctor who has to make a decision for a specific patient.

- The results obtained by formal methods depend on the data they use. Clinical data are tied with meaning, knowledge, data processing, data organization, etc. This data needs to be formalized in a way so that we keep its essential meaning in a particular clinical situation.

- Subjective information should not be ignored. Instead, more attention should be paid to the formalization methods of individual knowledge.

Specialists in machine learning and probabilistic modeling dealing with clinical applications point out the insufficiency of machine models alone and "the risks of the unwary use of data sets" [5]. Druzdzel and Diez in [5] claim that "it is necessary to resort to human experts' knowledge".

Let us give some examples from the literature of the common uses of expert knowledge.

- Expert interviewed by knowledge engineer who organizes the information elicited from the expert into a collection of rules
- Expert estimates
- Physician giving his opinion on the significance of a specific region on the ROC curve [6]
- Physician taking part in defining the graphical structure of a model (in Causal Probabilistic Models) [5,7,8,9]
- Physician describing explicitly the reasons that led him to make a certain diagnosis or recommend a certain therapy [10]

Our method for adequate formalization of clinical experience extensively uses an original technique of DGs [3], a powerful tool for clinical experience elicitation. We want to point out that the use of DGs in our method is radically different from traditional "expert knowledge" approach. In fact, our approach differs from all other proposed approaches in the following ways.

- We elicit particular types of medical knowledge - clinical experience, implicit knowledge, tacit assumptions - i.e. what is called "knowing-in action" [11]
- We do not just elicit knowledge from the clinician which might be ambiguous. Our actual goal is the construction of an adequate formalized language using elicited experience.
- Adequate language of this kind consists, roughly, of structural units and rules.
- Resulting formalized language is well founded both with respect to the logic and the actual meaning of the clinical situation considered.

3. Stages of Adequate Formalization Method

The important thing to know about Adequate Formalization (AF) method is that some of its stages are developed in parallel and some in sequential order. DGs are used in most of them. Because of size limitations we cannot describe here in detail all the stages of AF and point out their essential interrelations. We outline them below.

**Formalization of a problem statement:**

- A path: medical aim → medical decision problem(s) → formal decision problem of the given study
- Description of a group of patients
4. Adequate Formalization in the study of the Differential Diagnosis of Purulent Meningitis in Infants

It is well-known that the choice of an adequate treatment of a purulent meningitis depends on its etiology. The goal set for the DG carried out in the early stage of this study was defined as followed: using clinical picture of the illness the expert physician had to determine the etiology of meningitis².

Analyzing this DG it became clear that the pattern of the onset of the illness was relevant to its etiology. In the DGs that followed, the expert repeatedly came back to assessing the acuteness of the progression of illness using expressions such as "acute onset", "subacute progression of the illness", "undulating illness course" etc. However, formulating any formal criteria proved practically impossible at that point. In particular, the impediment to formalized assessment of illness onset lay in the fact that the information concerning the illness onset was communicated by patient's parents. Evidently, such information may have been incomplete and self-contradictory.

In order to find the formal criteria that indicate the illness onset a thorough application of the adequate formalization method was performed. As the first step it has proved important to understand and to express formally the notion "The first day of illness" as a formalized feature (about the two levels of formalization see [3]).

It is important to know that, in the later stages of formalization five types of illness onset were singled out and have contributed to the elaboration of adequate language concepts. These became the basis for application of the formal rules.

In the next stage four structural units have been built [2] (two of them coincided with two types of illness onset). The solution of the problem has been obtained in the

² The authors must remind that this example serves only as methodological illustration and its medical meaning will not be discussed in the present paper.
form of a relatively simple algorithm based on those structural units. The prospective verification of the algorithm and its clinical impact evaluation gave meaningful and statistically significant results.

Here are the structural units for determining the etiology of meningitis for infants during the first year of life.
1. Evident neurological symptomatology.
2. Otitis
3. Slack prodromal period with catarrhal symptoms
4. Acute prodromal period of a nasopharyngitis type

Though structural units have a simple shape, some of them have complex internal structures. It is highly important that structural units

- are always expressed in a language that is understandable to physicians;
- do not require any additional interpretation at all;
- are formalized and therefore can be used in a computer algorithm.

These characteristics are essential for an adequate language.

The algorithm obtained in this study was formulated as a simple logical expression (equivalent to a Decision Tree) using structural units mentioned above. While the questionnaire elaborated in this work contained many dozens of low-level features, the resulting algorithm is compact and uses only 4 structural units from the adequate language vocabulary.

5. Novelty and originality of AF Method

Herein we list several essential features which define the novelty and originality of the method of adequate formalization.

- In the AF method, unlike in other approaches to formalization of experts' skills and knowledge, an elaboration of adequate description and discovery of structural units always precede construction of the algorithm. This is a radically different approach to formalization and modeling.
- The structure of the algorithm is usually rather simple. By contrast, the concepts of adequate language have often a complicated and non-trivial structure with respect to initial features.
- The AF method allows a drastic reduction of the feature space dimension. Only then, the algorithm is applied to structural units.
- The result of the algorithm coming from the AF method does not require any interpretation. The algorithm is formulated in terms that could be applied to the individual patient.
- The AF method is applicable to small size samples when the initial dataset is insufficient for statistical analysis.

6. Limitations

As with any scientific method, it is important to indicate explicitly its limitations. The two most significant are as follows.

- The use of AF method is effective in those medical decision problems where sufficient clinical experience is available.
- Results obtained by the AF method are valid only in given clinical settings.
Conclusion

At a first glance, it might look like the results of AF method are not so helpful for a high level expert since in most cases, the expert makes right decisions. "However people often forget what great losses are borne by doctors and patients to attain this level of expertise" [12, p 6]. Such is the opinion of Professor AL Syrkin (Sechenov Moscow Medical Academy), a high level specialist in cardiology who participated in our studies and DGs for long years. By using AF method, young doctors gain in knowledge and experience. But high-level clinicians gain also: "after collaboration with high-level mathematicians, the clinician attains a new level of thinking" [12, p7]. This is valuable for teaching purposes. It allows knowledge and experience to pass to the younger generations of doctors.

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