CREATING DIAGNOSTIC CRITICAL APPRAISED TOPICS CATROM ORIGINAL SOFTWARE FOR ROMANIAN PHYSICIANS

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Abstract - *Diagnostic test assessment is large discussed in foreign languages medical literature and exists a significant number of programs, which dons well this task. Romanian physicians do not have too many choices when they want to proceed to diagnostic test assessment. This reason was conducted us to make a review on diagnostic test assessment theory and software implementation, and starting from this point to creates an original software for Romanian physicians. The present paper describes the part of the application, which allows physicians to operate with diagnostic test assessment. The application was creates on a client-server system, which allows simultaneously secured access of the Critical Appraised Topics database.*

Keywords - *evidence-based medicine, critical appraise topics, diagnostic test assessment*

Introduction

Evidence based medicine define as "the conscientious, explicit and judicious use of current evidence in making decisions about the care of individual patients" [1] has as core activity searching for and critical appraise the evidence on a specific clinical issues [2, 3, 4].

In day-by-day activity as physician, we make diagnosis decisions all the time. Diagnosis can be defines as the process of using patient history, physical examination, laboratory, imaging tools and other test to identify correctly the disease responsible for the patient's symptomatology. Knowing the diagnosis allows us to treat the patient and to give to our patient accurate information about prognosis. The most appropriate type of reasoning during the diagnostic process in practicing evidence-based medicine is the hypothetico-deductive, meaning generating and rejecting hypotheses as more data are collected. The hypothetico-deductive style involves proposing a differential diagnosis, asking a question, using the answer to refine the differential diagnosis, asking another question, again refining the differential, and so on until a final working diagnosis are obtains. In order to

perform the above-described activity of diagnosis some specific skills are necessary [1, 2]. First key skill for evidence-based practice is the ability to develop questions that can be answer using research evidence. Second, it is necessary to acquire skills that to allows finding evidence to answer our question, the most consuming part of evidence-based medicine. Third, is the critical appraise of the evidence. Finally but importantly, integrate the best evidence with the personal experiences and patient values and apply it in practice.

Evaluating an article on diagnosis test suppose to acquired knowledge in study design as well as basic statistics. There are three basic issues in an diagnosis paper assessment: validity (closeness to the scientific truth), relevance (usefulness to the practice), and results [5, 6, 7, 8, 9]. Articles about diagnosis can be of varying quality. Evaluating the quality of an article involves first to determine whether the procedure is feasible in our community. Even if the diagnosis test is the best one, if we did not have the device for example, or a physician able to interpret the results, the diagnostic test is unusefully for our practice. Looking also to relevance, the study population

should be reasonably similar to our patient. Ideally, the study should include patients with a spectrum of severity from mild to advance disease and without disease.

Assessing the validity of the information is an important task. The core key indicators of diagnosis study quality are presenting the diagnosis based on a golden standard, performing a blind test (the examiners which doing the test are 'blinded' to the golden standard results), performing the golden standard independent of the results of the studied test. Ideally, the data should be collects prospectively, because we cannot know how accurate the medical records are. Finally, the diagnostic test should be applies to a reasonable number (at least 100) of patients with an appropriate spectrum of disease (patients with mild, moderate, and severe disease as well as patients with similar symptoms).

The results of the study must be evaluates in order to decide if the diagnosis test is an accurate one. The simplest diagnosis test results are dichotomous when the patients can be classifying according to the presence or absence of disease. In this case, a lot of key parameters of interest can be compute in order to measure the effect size of the diagnosis test: sensitivity, specificity, predictive positive value, negative predictive value, pretest probability, posttest probability, pretest odds, posttest odds, positive and negative likelihood ratios and so on [2, 10, 11, 12]. Evaluating the results of a diagnosis test suppose to look at the point estimation of the parameters and to interpret its confidence intervals which can provide information about the trustworthiness or robustness of the finding [13].

When a diagnosis paper is critically evaluates, would be a waste of time if we will not summarize the information in order to be available another time or by other physicians. Summarizing the relevant information on a standardized model is knows as Critical Appraised Topics (called CAT) [14]. Correctly create diagnostic critical appraised topics became a useful tools for day-by-day activity.

The aim of this paper is to present the CATRom original program that allows Romanian physicians to create diagnostic critical appraised topics.

Materials and Methods

Creating a critical appraise topic can be divides into two parts: one for effective creating the CAT and another for management of information, components that can be see in our application.

A MySQL database [15] was develops to managing CATs from all medical domain (even if we talk about therapeutic studies, diagnosis studies or studies of association between risk or prognosis factors and disease) by Romanian physicians. The database is called `gpm` and software CATRom and are hosted in academicdirect.ro domain. The `gpm` database contains two tables called `subi` and `user` respectively. Both tables are primary tables. The `subi` table contains all information include into a critical appraise topic and have the fields `id`, `nume`, `titlu`, `data`, `tip`, `intrebare`, `pacient`. The `id` field is a primary key automatically generated using the auto_increment feature of MySQL database server. The `name` field store the name of the physician which creates the subject. The `titlu` field store the title of the subject and allows 250 characters. The `data` field store the data when the subject was create, is automatically set using the server system clock time, and have the next structure: YY.MM.DD.HH.MM.SS. The next two fields, `intreb` and `pacient` are medium text type (it stores till 224+3 bytes). The `intreb` field store the first part of the critical appraise topic (the question that can be answer using research evidence, the search terms and the reference to the best evidence that allows to answers to the question), while the `patient` field contain the second part of the subject (the information that allows to assess the relevance, validity and results).

Note that the `subi` table are designed to store all study domains (treatment/therapy, diagnosis/ screening, and etiology/prognosis). The structure of the information stored in the `patient` filed is different for each study domain and will be described latter. The `user` table contains three core fields, represented by the `id` field, the `name`, and the `pass` fields and other information use for database administration. The physician password is encrypted.

The visible part of the application consists of the client interface, which mainly reefers to critical appraise topic creation. Behind this

interface are HTML (Hyper Text Markup Language) markers and scripts. For the user interface, the PHP programming language was used. Using the HTTP address of the program (mentioned in the results section) on an Internet browser, the application displays a web page with menu and all instruction in Romanian language. The menu has designed with feature of Multilanguage support. In the application there are some parts that are commune to all three study domains (treatment / therapy, diagnosis / screening, etiology / prognosis) represented by the first page, login page, and the page where the title, the clinical questions, the search terms and the reference are submitted. The client interface work with a number of nineteen core programs that are common to all three medical domains.

The common interface in creating a new critical appraise topics must include the translating the need of knowledge in an answerable question (see figure 1 from Results section). First, a new CAT it have a title and the meaning of the title must be significant for the content in order to be usefully because it is uses in selections. The interface must contain the essential components of question:

• The patient and/or problem of interest;
• The main intervention (define very broadly, including an exposure, a diagnosis test, a prognostic factors, a treatment, a patient perception, …);
• Comparison intervention (if is relevant);
• The clinical outcome(s) of interest.

The key terms used in searching the best evidence that allows to response to the clinical question and the reference based on that the critical appraise topic is need on this stage of CAT creating.

Now the application interface is different and depends on the type of the subject domain. The cores structure follows the description of the design of the study, the characteristics of the patients, the results, and comments and are creates based on a comprehensive study of medical informatics literature. All above-describe characteristics will help physicians to critically appraise the article.

The diagnosis/screening study design interface can contains a drop-down list from which the user can select the type of the study: case control study, cohort study, cross sectional study, and experimental study (simple or double blind). Also in study design section, there are three statements (it can be answer with 'Yes', 'No', or 'not known'): 'There was an independent comparison with a reference standard', 'The reference standard is applied independently of the test being studied?', and 'The new diagnosis test is reproducible?'. Our CATRom implementation obeys this design (see figure 2).

The characteristics of the patients in a diagnosis/screening study contains the total number included in the study, the criterions of inclusion and exclusion in the study, the characteristics of the case and control groups, description of the new diagnosis test and of the standard test, and the similarity from the case and control groups.

The structure of results is designs on 2×2 contingency table were the number that corresponds to the real positive (noted with a), real negative (noted with d), false positive (noted with b) and respectively false negative (noted with c) cases must be fills. Based on the contingency table, the application computes all diagnostic key parameters used in assessment of a new diagnosis.

A number of twenty key parameters are computed: sensibility, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, prevalence, probability of a positive test wrong, probability of a negative test wrong, probability of a positive test, probability of a negative test, overall accuracy, false positive rate, false negative rate, pre-test odds, post-test odds, post test probability, odds ration, relative risk, and differences of proportions.

First three parameters calculated by our software from the contingency table data are Yates-corrected chi-square test value and associated p-value and Phi-statistic. Note that the appropriate measure of association for a 2 X 2 table like TD(diagnostic test)/B (disease) table is a Phi, which is derived by dividing the total chi-square value of the table by the total number of observations and then taking the square root of the result:

$$\chi^2 = \frac{(a+b+c+d)\left(|ad-bc| - \frac{a+b+c+d}{2}\right)^2}{(a+b)(c+d)(a+c)(b+d)} \qquad (1)$$

where a = TD$^+$B$^+$, b = TD$^+$B$^-$, c = TD$^-$B$^+$, d= TD$^-$B$^-$ (see figure 2). The p-value results from chi-squared distribution (2) and phi-statistic is defined by (3):

$$\chi^2_{obs} = \chi^2(p,1) \qquad (2)$$

$$\phi = \sqrt{\frac{\chi^2}{a+b+c+d}} \qquad (3)$$

All medical key parameters are accompanies with confidence intervals limits. The values of confidence limits calculation is the subject of a mathematical approach which is detailed in a series of papers [16, 17, 18, 19, 20, 21].

All necessary characteristics of the study design are included as well as the information stored in the contingency table. If exists empty obligatory fields in the second form (figure 2) and the 'Finalizeaza' button is pressed, the application displays the name of the field that is necessary to be filled and allows to go back. If all-important filed are completed, pressing the finalize button will display a summary of the critical appraise topic and allows to verify the included information. After checking up the information, the 'Inregistreaza' button allows to record the information in the database. After recording the information, the text of the subject cannot suffer changes. The idea there is that when a subject become deprecated, is possible to delete the record and create a new one.

Because usually diagnostic studies do not present all medical key parameters based on the contingency table values, we chouse to recalculate all medical key parameters based on contingency table and present them together with their confidence limits. This is one of the main facilities, which our software provides (table 1).

No	Medical key parameter	Nickname in the program	Confidence interval function	Ref.
1	Difference of proportions	ExcesRisc	DAC	[21]
2	False Negative Rate	RataFalsiNegativi	Binomial	[16]
3	False Positive Rate	RataFalsiPozitivi	Binomial	[16]
4	Negative Likelihood Ratio	RatieProbabilitateNegativa	RPAC2	[20]
5	Negative Predictive Value	ValoarePredictivaNegativa	Binomial	[16]
6	Odds ratio	RataSansei	R2AC	[19]
7	Overall Accuracy	Acuratete	Binomial	[16]
8	Positive Likelihood Ratio	RatieProbabilitatePozitiva	RPAC2	[20]
9	Positive Predictive Value	ValoarePredictivaPozitiva	Binomial	[16]
10	Post Test Odds	SansaPostTest	Binomial	[17]
11	Post Test Probability	ProbabilitatePostTest	Binomial	[18]
12	Pre Test Odds	SansaPreTest	Binomial	[17]
13	Prevalence	Prevalenta	Binomial	[16]
14	Probability of a Negative Test	ProbabilitateTestNegativ	Binomial	[16]
15	Probability of a Negative Test Wrong	TestNegativGresit	Binomial	[16]
16	Probability of a Positive Test	ProbabilitateTestPozitiv	Binomial	[16]
17	Probability of a Positive Test Wrong	TestPozitivGresit	Binomial	[16]
18	Relative Risk	RiscRelativ	RPAC2	[20]
19	Sensibility	Sensibilitate	Binomial	[16]
20	Specificity	Specificitate	Binomial	[16]

Table 1. Diagnostic key parameters and theirs confidence intervals functions

Results

The presented application is an original one, based on a comprehensive review of diagnostic assessment studies. After the literature reviewing, the proper information for diagnostic studies was selects and included in the designed application. The parameters of relevance, validity, and results of a diagnosis test mentioned in *Materials and Methods* section can be considered as results of present study. Anyway, the database stores it and can display as well.

The welcome page presents the main objectives of the application (figure 1) and allows to login to the database if the user has already an account. Otherwise, an interface conducts to define a new account. In addition, a button (called Ajutor) opens the help of the program. The procedure of inserting a new diagnostic assessment is made through the interface from figure 2.

Figure 1. New CATRom creating interface (first form, first page)

Figure 2. New diagnosis/screening study design interface (second form, second page) with CATRom

An interface for interrogating the CATRom database was build. The interface is available through 'Display' link (figure 3).

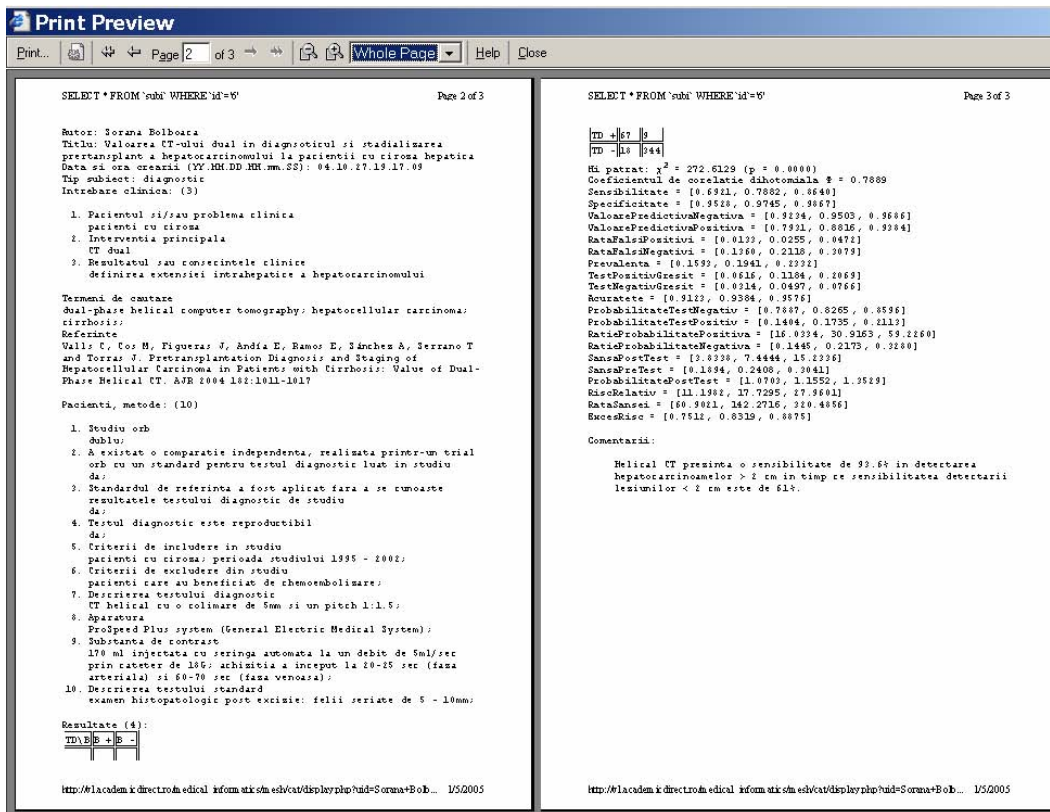Figure 3. Multicriterial sorting and selecting interface with CATRom

Figure 4. Prepared for print information from our CATRom software

The interrogating interface is multicriterial one. The sorting of displaying records can be dons by title ('titlu' link), author ('autor' link), domain of study ('tip' link), date and time ('data' link) and primary key ('id' link). The filtering of displayed records can be dons by title ('titlu' values links), author ('autor' values links), domain of study ('tip' values links), date and time ('data' values links) and primary key ('id' values links).

One of the most important results is the selection and summarizing the key parameters used in order to express the effect size of the diagnosis.

The application assembles the main operations referring to the CATRom manipulation: inserting CATs, deleting, filtering, and displaying. More, a user password-changing interface is also included. The results of the 'Display' link of the application for a given

CAT go to a prepared for print page with all study primary information and processed data (figure 4).

The application compute based on the data introduced by the user in the contingency table all diagnosis-type medical keys parameter referred in the literature. The computed key parameters are listed in table 1. Each point estimators is accompanies by confidence intervals limits, established after comprehensive studies (see refs from table 1 for more details).

Discussions

The presented application is a unitary interface for all medical domains, interface that allows displaying, creating, deleting, selecting, and changing users password and was created in order to help physicians in theirs day-by-day activity. Application allows creating, browsing, and deleting critical appraised topics being a useful tool in practicing evidence-based medicine. Using the application is possible just after crating an account, protecting the information store in the database.

The application was design for two kinds of users. First, for the physicians actively imply in creating the critical appraise topics (it is suppose that this category have high-level knowledge of English language, because almost all evidence are published in English; more, the users from this category it have insert and delete grants). Second, for the physicians who just use the critical appraise topic created by the first category.

Computing the all literature referred diagnosis keys parameters and theirs confidence intervals limits represents the main advantage of the application. As is already knows, that a confidence intervals is necessary in order to assess the trustworthiness or robustness of the finding [22]. Note that the most reported method of computing confidence intervals is the one that can easily be compute. The method that can be easy computes is never the best method. Our application use in computing confidence intervals laborious methods, most of them new ones, tested in providing better or equal estimations of confidence limits than reported ones [16, 17, 18, 19, 20].

Using MySQL database server and storing the data on a server give the possibility of using the information any time, at any hour and from any place in the country or all over the world. More than one user can read or write in our CATRom in the same time. A user can access the application if Internet connection is available and known to work with an internet browser. The database access, based on a login name and on a password, which is encrypts stored and can changed as many times as the user consider that is necessary.

The application allows printing directly from Internet browser as well as copying into Clipboard. Deleting a diagnostic critical appraise topic is allowed just for the user that created it.

CATRom application gives possibility of being at day with medical knowledge for a large number of Romanian physicians.

Conclusions

The application, dedicated for Romanian physicians, has a friendly interface that allows interaction with the users and can run on any computer that has Internet connection, offering an environment for diagnostic critical appraise topic creation. The application allows that a specific diagnostic critical appraise topic to be read in the same time by more than one user being a multitasking and multi-user application. The database access is protects by an encrypted password, and just the registered users can have access.

The quality of the critical appraise topic depend on the skills and knowledge of the physicians that create the topic and there familiarization with a Web browser. Including in the diagnosis critical appraised topic of all diagnosis key parameters allows physicians to filter the all information's that are necessary in diagnostic decisions.

Note that every new inserted topic is stored with the name of the physician that creates the topic, and the data of creation. The program can be use quite easy even by physicians that have the basic computer skills and it provide a useful tool for day-by-day practical activity.

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