

APPLICATIONS

## Creating Therapy Studies Critical Appraised Topics CATRom Original Software for Romanian Physicians

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**Abstract** - In day-by-day activity, physicians are face to therapeutic decisions all the time. They are influenced of the modality of presenting the results of a therapy study results from categorical data because depending on which measures of effect choused, the impact of an intervention may appear large or small, even though the underlying data are the same. Therapeutic key parameters obtained based on categorical data are debate in English and French medical literature and there are some programs, which compute parameters. Unfortunately, Romanian physicians do not have too many choices when they want to precede a therapy paper assessment. This reason was directed us to make a review on therapy 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 CATRom application that allows physicians to operate with therapy assessment. The CATRom implementation use a MySQL database for storing and managing information and PHP programming language for program interface. 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 therapeutic critical appraise topic creation. The quality of the therapeutic critical appraise topic depend just on the skills of the user who create it. Note that any evidence in therapeutic fields is change when new evidence becomes available and the therapeutic critical appraise topic must be periodically updated in order to be useful.

**Key words** – critical appraised topics, therapy studies assessment

### Introduction

In day-by-day activity as physician, we make therapeutic decisions all the time, making the same decisions most of the time. When we identify gaps on our therapeutic decision, maybe we ask for advice from a colleague or for an expert. Nowadays, when evidence-based medicine is a reality, we probably will not be comfortable with the above-mentioned approaches on therapeutic decision-making. Even if an opinion of an expert is very useful, it is necessary to remember that many experts live in a world very different from our own and their opinion is not always a feasible one.

Practicing a medicine based on evidence suppose to acquire some skills and to learn to use personal experience, which is a major

component of the art of medicine, in the interest of the patients. The practice of evidence-based medicine suppose to be able to translate the need of knowledge into answerable questions, track down the best evidence to answer them, appraise the evidence for its validity, and applicability, integrate that evidence with personal clinical expertise and apply it in practice, and evaluate our performances [1, 2]. Being able to assess an article on therapy is a necessity today. Evaluating therapeutic studies requires answering at three basic issues as in other studies: validity (closeness to the truth), relevance (usefulness in our clinical practices), and results [1].

The assessment of the validity supposes to look at the design of the study and to see the

possible systematic bias because we want an article that provides us valid results. The most valid study designs in considering a therapy are randomized clinical trials. After assessment of the validity, the evaluating of the relevance is necessary. Relevance relate to whether we can apply the results of the article to the care of our patients. First is important to decide if the treatment is feasible. If we are not able to procure the drugs, the treatment is irrelevant for our practice and we can ignore the article and try to find another paper. The last issue in assessment of therapeutic articles is to evaluate the results. Therapeutic articles can have two type of analysis: statistical and clinical. The statistical results are the p-values if the outcome variables are measured (quantitative variables) and medical key parameters with confidence intervals if the outcome variables are categorical. If we have categorical data, physicians can be influenced of the modality of presenting the results of a therapy study because depending on which measures of effect choused, the impact of an intervention may appear large or small, even though the underlying data are the same [3]. From these reasons, imply to have basic knowledge of statistics, knowledge that are not commune at Romanian physicians. Even that, the statistical analysis of a therapeutic study is necessary to undergo by rational filter and personal experiences in order to be clinical interpret. The medical literature can be full of statistical significant but clinically irrelevant results.

When a therapeutic article is critically asses, would be a waste of time if we will not summarize the information in order to be available another time when it is necessary to face to the same therapeutic problem. Summarizing the relevant information on a

standardized model is knows as critical appraised topics (called CAT) [4].

First component of a CAT are the title and a clinical bottom line describing a specific clinical problem, usually based on a foreground questions (a specific knowledge about managing patients with a disorder). Second component is represent by four level of foreground question: patient and/or problem, intervention, comparison intervention (if relevant), and clinical outcomes. Third component contain the search terms that were use to find the best evidence to answer to the clinical problem and the references to the articles. Fourth component is the study design and patient characteristics. Fifth component is a summary of the results, when these can be express as categorical data in a 2×2 contingency table. Sixth is the comment component where any important issues as adverse effects, costs, or unusual elements of the critical appraisal must be included [1, 4].

The aim of this paper is to present a friendly interface of a program that allows Romanian physicians creating a therapeutic critical appraised topic which to include all key parameter compute based on categorical data.

### **Materials and Methods**

Creating a therapy critical appraisal 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. The MySQL database implementation of the application was defined in a previously paper [5] as well as the PHP programs which allows interaction with the user. First of all, for the therapy assessment, in the entry interface ‘Tratament/Terapie’ item must be selected from ‘Domeniu’ drop-down list (figure 1).

Address [http://vl.academicdirect.ro/medical\\_informatics/mesh/cat/insert.php?uid=Sorana+Bolboaca\\_1](http://vl.academicdirect.ro/medical_informatics/mesh/cat/insert.php?uid=Sorana+Bolboaca_1)

[Afiseaza](#)    [Creaza](#)    [Sterge](#)    [Filtreaza](#)    [Parola](#)    Romana ▾

Data:     Autor:     Domeniu: Tratament/Terapie ▾

Titlul (max 250 caractere):

**Formulara întrebării clinice:**

Pacientul și/sau problema clinică:   
 Intervenția principală:   
 Intervenția de comparație:   
 Rezultatul sau consecințele clinice:

**Termeni cheie de căutare a evidențelor:**

Termen 1:     Termen 2:   
 Termen 3:     Termen 4:

**Referința către articolul pe baza căruia s-a realizat subiectul:**

Articol:

**Figure 1. Treatment/Therapy studies assessment selection using the CATRom interface**

Because the first form of therapy assessment is the same as for diagnostic/screening assessment, form that was presented in a previous paper [5] we will present here just the assessments of the relevance, validity, and results of a therapy intervention.

From the conceptual point of view, the assessment of a therapeutic study can be divided into four parts. First, and also the most important thing is the study design (clinical trial, case-control study, cohort study, systematic review, or meta-analysis). Each study design has associated a radio button, and the program allows to choose just one type of design. If the study is a clinical trial, it is necessary to specify if the study was double blind or not.

Second part contains the characteristics of the patients and the treatment where the number of the patients included in study, the inclusion and exclusion criteria, the description of the new treatment and of the placebo, the patients lost from the study, and similarity of the two groups of patients must be specified.

Third part of the form contains the results of the study organized as a T(treatment)\R(result) 2x2 contingency table. Based on data included into the contingency table fields, the application computes all point estimators and their confidence interval limits.

The last part of the form called 'Comentarii' can include the conclusion of the study, the adverse effect of the therapy and any

observation that can be made and which can be useful.

In medical studies where a treatment effect is measured as a categorical outcome, such as "efficacious" or "non-efficacious", a 2x2 contingency table can be created. The table contains four groups of cases: real positive cases (patients which receive the new treatment and at which the treatment was efficacious) noted usually with *a*; false positive cases (patients which receive the new treatment and at which the treatment has no effect), noted usually with *b*. The false positive cases (patients which receive a placebo drug and at which the outcome of interest was present), noted usually with *c*, and the true negative cases (patients which receive a placebo drug and at which the outcome of interest was not present), noted usually with *d*.

A number of seven distinct key parameters can be calculated and are reported into therapy literature based on the 2x2 contingency table. Our software computes all these parameters.

The application computes based on the data introduced by the user in the contingency table all therapy-type medical key parameters referred in the literature. The computed key parameters are listed in table 1. Each point estimator is accompanied by confidence interval limits, established after comprehensive studies (see refs from table 1 for more details).

No	Medical key parameter	Nickname in the program	Confidence interval function	Ref.
1	Experimental event rate	RataEvenimentExperimental	Binomial	[6]
2	Control event rate	RataEvenimentControl	Binomial	[6]
3	Absolute risk reduction	ReducereRiscAbsolut	ADAC	[7]
4	Number needed to treat	NumarNecesarTratat	IADAC	[8]
5	Relative risk reduction	ReducereRiscRelativ	ARPAC	[9]
6	Relative Risk	RiscRelativ	RPAC2	[9]
7	Odds Ratio	RataSansei	R2AC	[10]

**Table 1. Treatment/therapy key parameters and theirs confidence intervals functions**

The therapeutic key parameters [2, 3, 4, 11, 12], with associated nickname from our software are:

- Experimental event rate (EER) is the event rate in treated group:

$$\text{RataEvenimentExperimental} = \frac{a}{a + b} \quad (1)$$

- Control event rate (CER) is the event rate in control group:

$$\text{RataEvenimentControl} = \frac{c}{c + d} \quad (2)$$

- Relative risk reduction (RRR), the proportional reduction in rates of bad outcomes between experimental and control participants in a trial, calculated as:

$$\text{ReducereRiscRelativ} = |\text{EER} - \text{CER}|/\text{CER} \quad (3)$$

When the experimental treatment increases the probability of a good outcome, relative benefit increase (RBI) define as *the proportional increase in rates of good outcomes between experimental and control patients in a trial*, can be calculated as:

$$\text{CrestereBeneficiuRelativ} = |\text{EER} - \text{CER}|/\text{CE} \quad (4)$$

When the experimental treatment increase the probability of a bad outcome, relative risk increase define as *the proportional increase in rates of bad outcomes between experimental and control patients in a trial*, can be calculated as:

$$\text{CrestereRiscRelativ} = |\text{EER} - \text{CER}|/\text{CER} \quad (5)$$

- Absolute risk reduction (ARR) is the absolute arithmetic difference in rates of bad outcomes between experimental and control participants in a trial, calculated as:

$$\text{ReducereRiscAbsolut} = |\text{EER} - \text{CER}| \quad (6)$$

When the experimental treatment increases the probability of a good outcome, absolute benefit increase define as *the absolute arithmetic difference in rates of good outcomes between experimental and control patients in a trial*, can be calculates as:

$$\text{CrestereBeneficiuAbsolut} = |\text{EER} - \text{CER}| \quad (7)$$

When the experimental treatment increase the probability of a bad outcome, absolute risk increase define as *the absolute arithmetic difference in rates of bad outcomes between experimental and control patients in a trial*, can be calculated as:

$$\text{CrestereRiscAbsolut} = |\text{EER} - \text{CER}| \quad (8)$$

- Number needed to treat (NNT) = the number of patients who need to be treated to achieve one additional favorable outcome, calculated as:

$$\text{NumarNecesarTratat} = 1/\text{ARR} \quad (9)$$

When the experimental treatment increase the probability of a bad outcome, number needed to harm define as *the number of patients who, if they received the experimental treatment, would result in one additional patient being harmed, compared with patients who received the control treatment*, can be calculated as:

$$\text{NumarNecesarDauna} = 1/\text{ARR} \quad (10)$$

- Relative Risk (RR) defines as the ratio of risk in the treated group (EER) to the risk in the control group (CER). The RR is use in

randomized trials and cohort studies and is calculates as:

$$\text{RiscRelativ} = \text{EER}/\text{CER} \quad (11)$$

- Odds Ratio (OR) is defining as is the odds of an experimental patient suffering an event relative to the odds of a control patient. The odds ratio is use in case-control studies and is calculated as:

$$\text{RataSansei} = a\text{-}d/(b\text{-}c) \quad (12)$$

## Results

The presented application is an original one, based on a comprehensive review of therapeutic assessment studies when the result of the therapy

is a categorical one. After the literature reviewing, the proper information for therapeutic studies was selects and is included in the application. The therapy parameters with theirs associated confidence intervals can be considered as results.

The CATRom software is hosted on academicdirect.ro domain and is available at [http://vl.academicdirect.ro/medical\\_informatics/mesh/cat/](http://vl.academicdirect.ro/medical_informatics/mesh/cat/). The design interface of the therapy CATRom is present in figure 2. As we can see, the name of the user, the data and time of creation, the title and the clinical question for which the CAT is create are insert from the first form (the clinical question forms, that is common for diagnosis/screening, treatment/therapy, and risk/prognosis factors).

**Figure 2. New therapy CATRom design interface**

The most important criterions for assessment the relevance, validity and results are present here. The software was creating in the way that important fields must be complete in order to finalize the therapeutic critical appraised topic. These fields were defines based on a

comprehensive literature study. If for example, the choose type of the study is clinical trial, the CAT could not be finalized if there is no specification about blindness. An example of a warning is present in figure 3.

**Figure 3. The warning interface for incomplete the important fields**

If all-important filed are completed, pressing the finalize button will display a summary of the therapeutic 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. The text of the therapy subject cannot suffer changes after recording the information. Note that just the physician who create the therapeutic critical appraise topic have the facility to delete it, being protect by encrypted password.

The manager of the database creates users account and for each user assigns a user name (because the user name is store in each CAT this is in fact the name of the physician) and an encrypted password. At first login, the physicians must to change the password in order to assure the protection of the data stored in the database, following the 'Parola' link. A new

windows is open, containing the user name, and two fields the old password and the new password. The new password is automatically updates in the database.

One of the most important results is the selection and summarizing the therapeutic key parameters used in order to express the effect size of the therapy. Based on the data introduced by the user in the 2x2 contingency table, the software computes a total number of seven distinct therapeutic key parameters: RataEvenimentExperimental, RataEvenimentControl, ReducereRiscAbsolut, NumarNecesarTratat, ReducereRiscRelativ, RiscRelativ, RataSansei. All medical key parameters are accompanies with confidence intervals limits (see figure 4).

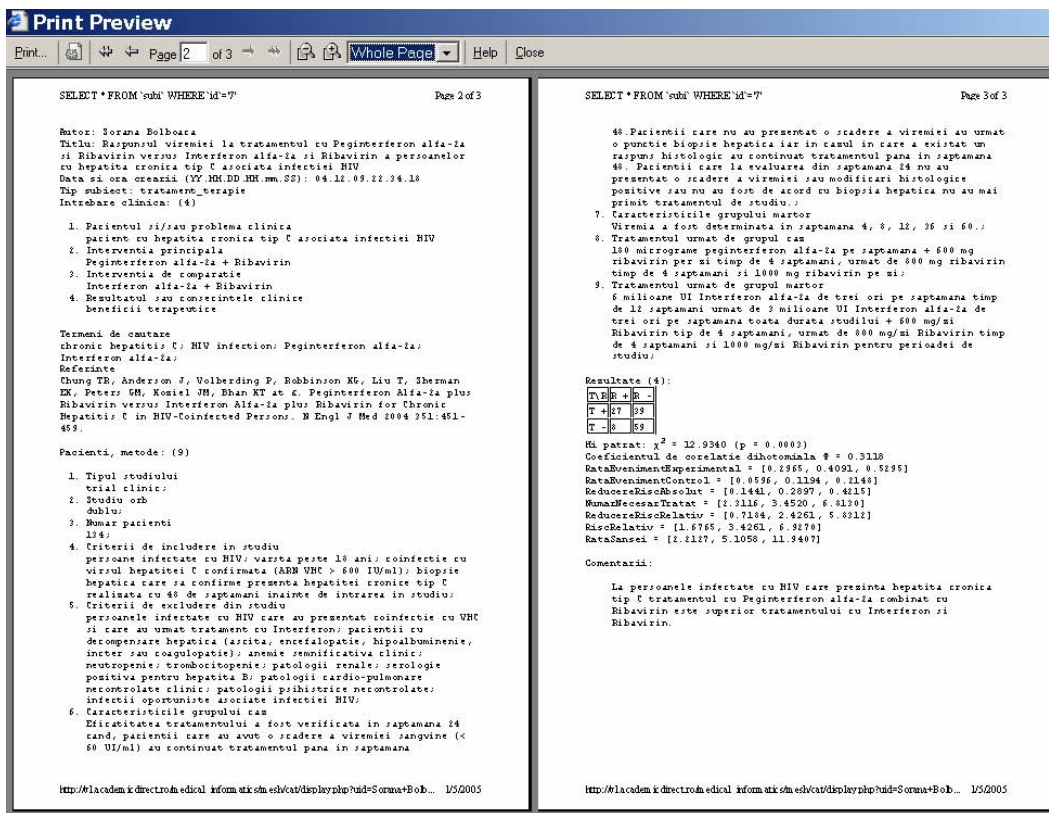


Figure 4. Prepared for print information from therapeutic CAT database

Because usually the results of therapeutic studies based on categorical variables do not present all therapeutic key parameters, we choose 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. The application assembles the main operations referring to the CAT 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 5).

### **Discussions**

There are some advantages of a critical appraised topic on therapeutic study for Romanian physicians. While most of the Romania physicians do not have high-level knowledge of English language and could not read an article in English, a therapeutic CAT created in Romanian language it will be a very useful tool in therapeutic decision-making activity. Once a therapeutic CAT was create it can be read as many time as it need, or next time when a similar clinical situation is necessary to be solve, reducing the documentation time. Much more, if the CAT is store into a database on a server, other physicians can read it, and the review of the CAT can easy be perform. It must be noted that the evidence are not static, they change when a better evidence become available and the CAT must be periodically updated in order to be a useful tools in day-by-day activity.

Application allows creating, browsing, and deleting critical appraised topics being a useful tool in therapeutic decision-making. Using the application is possible just after creating 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 all literature referred therapeutic keys parameters and theirs confidence intervals limits represents the main advantage of the application. As is well known, that physicians are influence of the modality of presenting the results of a therapy study because depending on which measures of effect choused, the impact of an intervention may appear large or small, even though the underlying data are the same. Our application gives possibility to observe and

interpret all therapeutic key parameters compute on categorical data providing useful knowledge for clinicians to balance the benefits and harms of therapy for their patients.

When is necessary to interpret a point estimator of therapy an estimation of the trustworthiness or robustness of the finding [13] is necessary, estimation which is give by the confidence intervals. ATLMAN [14] recommend that the confidence intervals should always be gives when a number needed to treat/harm is reports as study result. Note that just few papers report the therapeutic key parameter are accompanied by a confidence intervals and when is reported just the one that can easily be compute is referred. 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 [6-10].

The application allows printing directly from Internet browser. Deleting a CAT is allowed just for the user that created it. CATRom gives possibility of being at day with medical knowledge of therapeutic studies 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 therapeutic critical appraise topic creation. The application allows that a specific 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.

Computing all literature referred therapeutic keys parameters and theirs confidence intervals limits represents the main advantage of the application. Providing therapeutic parameters that are compute on categorical data accompanied by theirs confidence intervals, the application is a useful tool for therapeutic decision-making, giving to physician useful information for balancing the benefits and harms of therapy.

The quality of the therapeutic critical appraise topic depend just on skills of the user who create it. Note that the evidence in therapeutic fields are not static, it can be

change in one year or in one week. The evidence is change when new evidence becomes available and the therapeutic critical appraise topic must be periodically updated in order to be useful.

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