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INFORMATICS INSTRUMENTS USED IN EVIDENCE-BASED MEDICINE

Sorana Bolboacă, Andrei Achimăș Cadariu
Dept. of Medical Informatics and Biostatistics, University of Medicine and Pharmacy „Iuliu Hațieganu” Cluj-Napoca

Abstract - Nowadays, evidence based medicine is used more as a basis of medical practice in all medical specialties. Development of computers sciences and Internet communication allows the development, growing and spread of evidence-based medicine concepts and practice all over the world. We present in this paper some programs used in evidence-based practice in order to create, maintained and up-to-date the best medical reviews, creating and updating clinical practice guidelines, creating and maintaining critical appraised topics, storing and retrieving medical information tools, and assessing the health information quality. In order to practice evidence-based medicine, as physicians, we can choose now the software that is the best for our clinical needs. The conditions are to know English so good that to understand all we read and to be able to write correctly in English and of course to know how to use a computer and how Internet works.

Keywords: informatics tools, evidence-based medicine

Background
Until now, physicians, based on their clinical experience and their intuitions decided what clinical tests or what treatment any individual patient was need to followed. Now, physicians are encouraged to integrate best research evidence about diagnostic tests, prognostic and treatment with personal clinical experience and the patient value in their medical decisions. We are now in the era of evidence-based medicine.

As physicians, in order to practice a medicine based on evidence it is necessary to improve clinical knowledge, reading habits, and assessment abilities. Evidence-based medicine allows better communication with patients and more effective use of resources.

Nowadays, we confront with a rapidly expanding volume of primary medical research. In these conditions, medical literature review is becoming increasingly important to summaries research evidence. In contrast with traditional review that has been criticized for being subjective, scientifically unsound, and inefficient, systematic review could produce more reliable results by systematically locating, appraising and synthesizing research evidence.

Informatics Tools Used in order to Create Medical Evidence
There are many types of medical evidence. We will present below some programs, which allow us to create, and maintained reviews, guidelines and critical appraised topics. We will also present some statistical analysis software for research synthesis.

A. Preparation and updating medical reviews
We know that there are three type of review:

- Simple review is a review article in the medical literature, which summarizes a number of different
studies and may draw conclusions about a particular intervention.

- Systematic review is a review of a clearly formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research and to collect and analyze data from the studies that are included in the review. A review may or may not use statistical methods in order to analyze and summarize the results of the included studies.

- Cochrane review is a systematic review, up-to-date summary of reliable evidence of the benefits and risks of healthcare.

We need systematic review to efficiently integrate valid information on which we can make rational medical decision. [v] The use of systematic and explicit methods in review limits bias and reduces chance effects in order to provide more reliable results upon which to draw conclusions and make decisions. [vi, vii]

A1. Review Manager - RevMan

The RevMan [viii] software is a program created in order to help Cochrane reviewers to be systematic and comprehensible about questions they need an answer and make proper decisions about methods they use.

The RevMan software is developed at The Nordic Cochrane Center in order to help reviewers in constructing reviews in the appropriate format and to prepare files required to transfer reviews electronically. For a review to be called a “Cochrane Review”, it must be in The Parent Database, maintained by the Cochrane Collaboration. The Parent Database is composed of the modules of reviews submitted by Collaborative Review Groups registered with The Cochrane Collaboration.

RevMan allows us to:

- Enter review protocols;
- Complete reviews (including text, characteristics of studies, comparison table and study data);
- Perform meta-analysis of the data entered and present the result graphically.

The main window of RevMan has a Tree view structure, the menu bar and the toolbar (fig. 1). The menu bar contains the next menu: File, Edit, Action, View, Window and Help. The toolbar allows us to Print, Cut, Copy, Paste, Add, Edit and Delete, a pair of browse buttons and buttons for accessing the analysis program and the help file.

Figure 1. The menus and the toolbar.

Tree view is a structured representation for the reviews and their content (fig. 2) and allows us to manipulate them. This window cannot be closed.
The *Text of review* window is designed to enter and edit the text of the review. This window has pre-defined headings that are fixed for all Cochrane reviews and cannot be deleted or modified. In order to create a review with RevMan we can use bulleted lists, bold, italics and underline, superscript, subscript, mark the selected text, insert symbol, but we cannot use other formatting as tables, text justification, tabs, different font, etc. The program also allows us to find, remove, delete and insert link.

An important tool of the program is Analysis options that allows us to perform a meta-analysis of the data introduce in the review. Meta-analysis, the use of statistical methods to summarize the results of independent studies, can provide more specific estimates of the effects of healthcare than those derived from the individual studies included in a review. [6, 7, 8]

The meta-analysis of RevMan software is a cumulative one because the studies are added one at time in a specified order, for example according with the publication data or according with the quality of the study, and the results can be summarized as each new study is added.

According with the type of data, RevMan dispose the specific statistical method present in the Table 1.

<table>
<thead>
<tr>
<th>Type of data</th>
<th>Summary Statistic</th>
<th>Model</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>dichotomous</td>
<td>odds ratio</td>
<td>fixed effect</td>
<td>Peto</td>
</tr>
<tr>
<td></td>
<td></td>
<td>random effects</td>
<td>Mantel-Haenszel</td>
</tr>
<tr>
<td>relative risk</td>
<td>fixed effect</td>
<td>Mantel-Haenszel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>random effect</td>
<td>DerSimonian and Laird</td>
<td></td>
</tr>
<tr>
<td>risk difference</td>
<td>fixed effect</td>
<td>Mantel-Haenszel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>random effect</td>
<td>DerSimonian and Laird</td>
<td></td>
</tr>
<tr>
<td>continuous</td>
<td>weighted mean difference</td>
<td>fixed effect</td>
<td>inverse variance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>random effect</td>
<td>DerSimonian and Laird</td>
</tr>
<tr>
<td>standardized mean difference</td>
<td>fixed effect</td>
<td>inverse variance</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>random effect</td>
<td>DerSimonian and Laird</td>
</tr>
<tr>
<td>individual patient data</td>
<td>odds ratio</td>
<td>fixed effect</td>
<td>Peto</td>
</tr>
</tbody>
</table>

Table 1. Statistical methods used by Review Manager program.

The program it is also able to display graphical representation of the analysis, graphics that can be saved and used in other publications. The types of the graphical representation are Funnel Plot.

RevMan is a useful program which report the reviewers work explicit and concisely. The structure of the program it is flexible enough to fit different types of reviews (those with a single comparison, multiple comparison or those using individual patient data). RevMan generate reports that are informative and readable and can be viewed on a computer monitor or which can be printed. A great advantage of the program is that the review can be updating quickly.

Even if it is a great program for creating and maintaining Cochrane reviews, it is important to know that the software is not a replace of medical good judgments. The programs are address to Cochrane reviewer and the quality of review depends on the reviewer medical judgment.

RevMan is distributed as copyrighted freeware. Can be used and copied free as
long as no changes are made to the contents of the distributed package.

A2. Module Manager - ModMan
Module Manager is an extension of RevMan. The program was designed in order to allow the Collaborative Reviews Group to prepare their modules. Module is the paper prepared by a Collaborative Review Group in order to be published in The Cochrane Library. A module is consisting of the Collaborative Review Group details and the protocols and reviews that have been approved for publication in the Cochrane Database of Systematic Review. ModMan is software that can be used by a specific part of a population, the Cochrane reviewers. Can be downloading free from the Cochrane Collaboration Web site. [xii]

A3. MeerKat
MeerKat is software developed for individual Review Groups by the Update Software for the Cochrane Collaboration. The program allows organizing and maintaining the specialized register of studies for possible inclusion in systematic reviews carried out by Review Groups. The program allow to:
- Link citation to reports of studies;
- Link reviewers and their reviews to citations and studies;
- Export data;
- Import existing registers.
The minimum require to the MeerKat is the Microsoft Access at least 2000 installed on your computer. The program is create in order to be used by a specific part of medical staff, the one which is member of a review Groups. There are no taxes for using the program and the program can be finding on The Cochrane Collaboration Web site. [xiii]

B. Guideline
Clinical practice guidelines are designed to assist clinician and patient decision about appropriate health care for specific clinical circumstances. Simple publication of guidelines usually fails to change the behaviors of clinicians. [xiv] Guideline implementations involve education and feedback outside the clinical encounter setting. [xv]

B1. Shiffman Computer Guideline Implementation
Richard Shiffman and all, from Center for Medical Informatics, Yale School of Medicine describe a model for computer-based guideline implementation. They had identified eight critical information management services that can promote guideline integration into clinical practice [xvi]:

- **Recommendation** services determine the appropriate guideline-specified activities. Ideally, guideline statements can be represented as multiple if ... then rules. Each rule specifies antecedent decision variables and their corresponding states that initiate one or more system or end-user actions.
- **Documentation** services involve data collection as collection, recording, and storage of observations, assessment, and interventions related to clinical care.
- **Registration** services record and store administrative and demographic data. This part of the program provides patient-specific data collection and advice.
- **Explanation** services enhance the credibility of automated recommendations by providing supportive evidence and rating the quality of evidence.
- **Calculation** services measure time intervals, suggest medication dosages, and perform other computational tasks.
- **Communication** services provide rapid, accurate and widely accessible electronic message transfers that facilitate information exchange among clinicians, between the
laboratory and clinicians, and among administrative entities.

- **Presentation** services facilitate understanding of complex data, clarify trends, and format written, as prescriptions, for patients.
- **Aggregation** services associate outcomes with specific guideline interventions. Aggregation derives population-based information from individual patient data and can help validate or invalidate guideline statement or profile the adherence of providers to specific guidelines.

This information management services model offers a framework to promote work integration for development and evaluation of computer-based guideline implementations.

The program is designed for a specific medical population, the one that are involved in creating guidelines. You can obtain a copy of the program if you send a request mail to Richard Shiffman.

### B2. Transforming Guideline Information into Guideline Elements Model – GEM Cutter

GEM Cutter is a program developed by a research team from Yale Center for Medical Informatics. The tool is intended to facilitate the transformation of guideline information into Guideline Elements Model (GEM) format. GEM is a model developed in order to organize guideline information into a standard structure. GEM files are *.xml documents and can be displayed and manipulated for:

- Guideline quality assessment;
- Guideline dissemination;
- Guideline implementation.

The main window of the program is divided into three segments (fig. 3) represented by:

- **Guideline Text Segment:** contains the original guideline text.
- **GEM Tree Segment:** displays the contents of the GEM document in tree structure format. Every item in the tree represents a GEM Element.
- **Element segment:** contains a name bar, element source bar and element text box.

#### Figure 3. GEM Cutter screen. a. guideline text segment, b. GEM tree segment, c. element segment.

In order to create a GEM structured guideline, using some special tools, the program allows moving the text from the guideline text segment into GEM structured segment or manually editing text in this structure. The GEM Tree Segment structure is a standard one and cannot be edited or move or delete it.

GEM Cutter runs on any computers that have Windows 98, Me, NT 4.0, 2000 or XP. The .Net Framework is necessary to be installed in order to run GEM Cutter Installer.

GEM Cutter can work just with *.rtf and *.txt files. The integration of the information from guideline into a GEM structure is operator dependent.
The program it is easy to use if you are familiar with computer software and can be freely downloads from the Yale Center for Medical Informatics Web page. [xvii]

C. Creating and Maintaining Critical Appraised Topics

C1. CAT Maker

CAT Maker is software developed at the NHS R&D Centre for Evidence Based Medicine in Oxford, United Kingdom. The program helps us to create critical appraised topics for articles about Therapy, Diagnosis, Prognosis, Aetiology/Harm and Systematic Review of Therapy.

The program contained three main components:

- A textual guide to CAT’s (What’s a CAT? and What do CATs do?);
- A structured input sequence for making CATs for Therapy, Diagnosis, Prognosis Aetiology/Harm and Systematic Review of Therapy. The sequence are different structures for different CATs and allows automates calculation of clinically useful measures and their 95% confidence intervals.
- A section of critical Appraised Guidelines to help us identify the key features of the study we are working with.

The program allows us to save the CAT in three forms:

- If we are not finish with the construction of the CAT, we will save out work as Unfinished Kitten;
- If we are finished our work, we can save as:
  - A standard text file: *.txt;
  - An HTML file or WebCAT: *.html (in this situation we need a Web browser as Netscape or Internet Explorer to open them).

CAT Maker is easy to use, have a friendly interface and allows interactivity with users. The producer put to our disposition a demo version called CATnipper which provides all the functionality of the CATmaker, but this version will not give us access to all of the guides, and is time-limited (has just only nine lives). The license for a single user is 90£ and a site license which allows unlimited number of user is about 250£. [xvii]

C2. Cat Maker Online

Cat Maker Online is software developed by Christopher Dawes from Centre for Evidence Based Medicine. [xix] The program allows writing many types of critically appraised trial and share the editing and results with other people.

There are two version of Cat Maker Online:

- The Internet version: it is used when we have a fast permanent Internet connection, a good web browser (as Internet Explorer 5/6 or Netscape 6), and if we use Cat Maker Online infrequently.
- The Your Computer version: is better to use when the above condition are not accomplished and if we use Cat Maker Online often.

Installation and running required a software named JAVA. When we used the program for the first time, it is necessary to create a user and a password.

Cat Maker Online has a standard interface created in order to structure the CAT. The main window presents four navigation buttons (Question, Patient/Methods, Results and Other Stuff) which allows us to move from a window to another and a standard group of fields for editing. The Question and the Other Stuff windows are standard one but the structures Patient/Methods and Results windows are different if we want to create a CAT based on a Systematic Review of Therapy, Randomized Control Trial, Case-Control or Cohort Study, Prognosis or Diagnostic Study. On the base of the data introduce in the CAT, the program compute some statistical parameters and their 95% confidence interval.

At the end of editing process, there is an option that allows to share the CAT “Cat is published” on Global Medical Knowledge Database (the website has an intelligent search engine built into it that allows the
user to find CAT’s). The CAT can be saved as a *.html file or can be exported as an *.xml file.

Even if there are limits on the number of characters, which it allows to type into a file, the program is a useful one because it is very easy to use and create structures CAT that can be shared with other people all over the world.

D. Statistical analysis software for research synthesis

In the last few years, computer software entirely devoted to meta-analysis has increasingly become available, and meta-analysis procedures have been introduced in general statistical software packages. We will present some and briefly review of that software, providing a comparative summary of features (table 2).

<table>
<thead>
<tr>
<th>Comprehensi ve Meta-Analysis</th>
<th>MetaWin</th>
<th>EasyMA</th>
<th>Meta- Analyst</th>
<th>STATA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Version tested</td>
<td>2</td>
<td>2</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Operating system</td>
<td>Windows</td>
<td>Windows MS-DOS Windows</td>
<td>Windows</td>
<td>Windows, Macintosh, Unix</td>
</tr>
<tr>
<td>Price</td>
<td>995$ / 595$</td>
<td>150 $ for one user</td>
<td>free</td>
<td>250$</td>
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<td>Statistical models</td>
<td>Fixed effects Random effects Inverse variance Schmidt-Hunter test</td>
<td>Comparing two mean Odds Ratio Risk difference</td>
<td>Fixed effects Random effects</td>
<td>Fixed effects Random effects</td>
</tr>
<tr>
<td>Test for homogeneity</td>
<td>no</td>
<td>yes</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Manual</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Disadvantage</td>
<td>Necessary to be familiar with computer program. The price for Comprehensive Meta-Analysis is a little bit too high for Romania.</td>
<td>The program menus are in English but the help menu is in French. It is not allowed to export the plots.</td>
<td>Allows to analyze dichotomial data from randomized clinical trial. It is not allowed to export the plots.</td>
<td>The price it is a little bit high.</td>
</tr>
</tbody>
</table>

Table 2. Summary of features of four meta-analysis software packages.
Evidence-Based Databases - Storing and Retrieving Medical Information

1. InfoRetriever

InfoRetriever is an informatics tool created and maintaining by POEMS (Patient Oriented Evidence that Matters). The program was designed in order to place evidence-based decision-making tools at the clinician's fingers. It is a big database system, which contains a lot of filtered and synopsized evidence-based information and tools:

- Abstracts from POEMs (over 2000 critical appraisal of primary care articles with other 100-350 added annually) and Cochrane Systematic Review (over 1500 abstracts of systematic reviews other hundred added annually);
- More than 120 decision supported tools;
- More than 1800 details data of diagnostic tests and maneuvers;
- Over 80 clinical decision rules;
- Over 400 practice guideline;
- Concise, clear summaries of over 1100 clinical topics from Griffith's 5-Minute Clinical Consult including over 500 photos;
- Basic prescription information on over 1100 drugs, including use in pregnancy and lactation.

The best way to use InfoRetriever program is to search the information that you need. For this, it is necessary to enter a term to search; the database matches your terms to relevant keywords. If we select one or more keywords the program it will display the results. Results are organized by:

- The type of information (treatment, diagnosis);
- Level of evidence (from 1 to 5);
- The source of evidence (InfoPOEMs, clinical rules, Cochrane Database).

The program is a very useful one on day-by-day clinical practitioners and it is available for desktop, laptop, handheld computers, and the Web. The minimum required is a Pentium II 300 MHz, and operating system Windows 95/98/2000/Me/XP.

The developer put on your disposition a Trial Access that can be use it for 30 days. After that, the program it will shout down unless we do not obtain a new registration. The purchase can be an Institution/Hospital/Residence/Group Practice or an Individual Practice one. The acquisition price of the program is between 247€ and 450€.

2. Cochrane Library

Cochrane Library is a collection of resources designed by Cochrane Collaboration, published on a quarterly basis and available on CD-ROM or the Internet. The aim of this library is to bring together in one place reliable information that can be used in medical decision. The Cochrane Library consists of several resources that can help practitioners and consumers access reliable up-to-date information:

- The Cochrane Database of Systematic Review (CDSR): full-text systematic review of effects of health-care interventions in pregnancy and childbirth, stroke, schizophrenia, and increasing range of specialties.
- The Database of Abstracts & Reviews of Effectiveness (DARE): structured abstracts of high quality published systematic reviews.
- The Cochrane Central Register of Controlled Trial (CENTRAL): is the Cochrane Collaboration's register of controlled trials, which provides bibliographic information (i.e. abstracts rather than full-text) on nearly 350,000 reports of trials identified by contributors to the Cochrane Collaboration.
- The Cochrane Controlled Trials Register (CCTR): bibliography of 150,000 controlled trials, many not listed in major biomedical database.
- The Cochrane Database of Methodology Reviews (CRMD): bibliography of articles on research methodology and preparing systematic review.

Accessing the Cochrane Library is possible by subscription. Some countries with
national provisions have purchased licenses for their residents to use The Cochrane Library without charge (e.g. Australia, Belarus, England, Ethiopia, Fiji, Finland, French Southern Territories, Ghana, Ireland, Kenya, Kiribati, Malawi, Marshall Islands, Mozambique, Nigeria, Norway, Palau, Papua New Guinea, Samoa, Sri Lanka, Tanzania, The Cook Island, Tokelau, Tonga, Tuvalu, Uganda, Vanuatu, Zambia). Annual subscription prices depend on which type of Cochrane Library you want to subscribe to:

- Online: a personal license is £155 and an organization site license for one user is £323, and it will be necessary to pay another £64 for each additional user.
- CD-ROM: a personal license is £155 and a CD network license for one user is £323, and it will be necessary to pay another £64 for each additional user.

Assessing the Health Information Quality

1. DISCERN

DISCERN is a program developed by a group consisting of clinical specialists, general practitioners, consumer health information expert, medical publisher, health consumer with the financial support from The British Library and the NHS Research & Development Program. DISCERN was designed in order to help health consumers and information providers assess the quality of written information about treatment choices for a health problem in order to take the best medical decision. It is organized in three sections as followed:

- Section 1 (questions 1-8) address the reliability of the publication and should help us consider whether it can be trusted as a source of information about treatment choices;
- Section 2 (questions 9-15) focuses on specific details of the information about treatment choices;
- Section 3 (questions 16) consists of the overall quality rating at the end of the instrument. Our answer at this question it will be based on our judgment of the quality of the publication as a source of information about treatment choices.

The DISCERN is a useful instrument which enable consumers and information providers to judge the quality of health information on treatment choices. The instrument cannot be used to assess the scientific quality or accuracy of the evidence on which the publication is based but can be used to judge the reliability of a publication as a source of information about treatment choices. DISCERN can be used without the need for a specialist knowledge, to judge the quality of publications about one particular treatment choice.

DISCERN can be used by organizations without permission if it is used according with the instructions and if the organizations experience is summarized into an evaluation form and sent a copy to the developers. [xxii]

2. Information Quality Tool

Information Quality Tool is an online tool created by Mitretek Systems in collaboration with the Health Summit working Group’s “Criteria for Assessing the Quality of Health Information on the Internet”. [xxiii] The aim of the program is to help consumers to evaluate the quality of Internet medical information.

The assessment is based on the answers of the reader to a number of 21 questions. The question type is closed (you can answer just with “yes” or “no”). The result of assessment is a perceptual number. A 100% site is the one which provide the best quality medical information.

The program is implemented in JavaScript, has a nice interface and it is easy to use by the one which is familiar with Internet Explorer. As disadvantage for Romanian consumers is that, they must to comprehend English because the assessment is based on consumer English knowledge.
Final comments
The software presented in this paper cover all the possible software that can be used in evidence-based medicine. For example, reviewers are different kind of software that allows creating medical reviews (RevMan), prepare modules (ModMan) or organizing and maintaining the specialized register of studies for possible inclusion in systematic reviews (MeerKat). All these free programs were created for a specific part of medical staff, that which is directly involved in creating systematic reviews. If the reviewers want to solve the statistical problem with another program than the free Cochrane programs, there are a lot of them at different prices and with different background and what program to choose depend on the financial possibilities and the capabilities of the software’s.
Clinical practice guidelines, books which are up-to-date at every 6 months, can be created and maintaining using a free program created by The Yale Center for Medical Informatics. If as physicians, we are interested in creating and updating critical appraised topics, we can use programs like CatMaker if we have the possibilities to pay 250£ for an unlimited number license or to use the Cat Maker Online software.
The numbers of medical databases are increasing day-by-day, and we can choose the best one for our needs and our financial situation.
Moreover, the last but not the least, we have possibilities to assess, as a physicians and as a patient, the health information quality using some free programs as Discern and Information Quality Tools.
Even there are many programs used in evidence-based medicine, there are some disadvantages for Romanian physicians. First, the Romanian physicians must to have strong English language knowledge in order to understand correctly the meaning of the problems and to be able to write in English correctly. Second, they must to know how to use a computer properly, how to access the Internet and strong strategies for searching medical evidence. If we will be able to pass this two barriers we can say that we will be able to practice an evidence-based medicine.

References:


