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Evidence-Based Guidelines Assisted Creation through Interactive Online Environment

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Abstract - In accordance with the national and international trend in creating the equitable, efficient and cost effective health care systems and with the Romanian healthcare reform, a tool for assisting creation of guideline models and evidence-based guidelines was developed and assessed by implementation of an evidence-based standardized guideline model. By the use of the MySQL and PHP features, an original evidence-based guideline developed methodology was implemented into the GUIDELINE(ONLINE) system. The application is hosted on AcademicDirect domain and is accessible at the following address: http://vl.academicdirect.org/medical_informatics/guidelines. The GUIDELINE (ONLINE) opens the pathway through creation of standardized guideline models and clinical practice guideline in native language.

Keywords - Practice Guidelines; Evidence-Based Medicine, Quality of Health Care; Online Interactive Application; Continuing Medical Education

Introduction

All over the world, improving the quality of health services and reducing the costs are nowadays the main objective of healthcare policies. Clinical practice guidelines define as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances” [1], are scientific instruments which has as objectives standardization of healthcare [2], and proved to improved the medical knowledge of practitioners [3], the quality of health care services [2], and decrease the costs of health care services [4]. As was remarked by Steinberg [5] “practice guidelines have become more rigorously evidence-based and are now packaged in ways that make it easier to put them into practice”. Despite the development of clinical practice standards [6,7], assessment instruments [8], and methodologies [9-11], the clinical practice guidelines have had limited effect on changing physician behavior, being limited by insufficient knowledge [12], individual acceptance of guidelines [13], outcome expectancy [14], the desire [15] and the ability to overcome the inertia of previous practice [16], the credibility of content [17], lack of time [18], interest [19], and involvement [20], and doctor-patient relationship [21]. Even if the

clinical practice guidelines are available, for Romanian physicians are inaccessible because most of guidelines are in electronic version and many physicians did not have access to a computer and to the Internet and in most cases the information are in English.

According with the international trend in creating the equitable, efficient and cost effective health care systems [22,23] and with the Romanian healthcare strategy [24], a tool for assisting creation of guideline models and evidence-based guidelines was developed and assessed by implementation of a evidence-based standardized guideline model.

Materials and Methods

Evidence-based Clinical Practice Guideline Methodology

After a comprehensive study of specialty literature and analyzes of accessible guideline methodologies existent at international and national level an original methodology which include thirty-nine elements was developed. The elements and their characteristic are in table 1. Six out of thirty-nine elements of evidence-based guideline methodology are used just for indexing propose of guideline into database.

Table 1. The methodology of the standardized evidence-based guideline model

No.	Element	Specification
1	Guideline title	The guideline title must express clear and concise its contents and must be short and accurate
2	Status	Type o guideline (new guideline, updated a previous created guideline, etc.)
3	Data	Data when the guideline was created
4	Organization	The name of organization or association responsible by guideline creation, and contact details
5	Updating	The date at which it is propose to update the guideline information
6	Disease	Contain the disease or diseases at which the evidence-based guideline is addresses to
7	Keywords	Specification by choosing from a list the MeSH descriptors
8	Domain	Specification by choosing from a list the domain or domains of guideline
9	Medical Specialty	Specification by choosing from a predefined list the specialty or specialties at which the guideline is address to. The list of medical specialties are in conformity with Ministry of Health Decree no. 197, 2004 February 23
10	Addressability	Specification by choosing from a predefined list the potential users
11	Aim	Description of the aim of the evidence-based guideline
12	Objectives	Specification of the objectives of guideline
13	Practical Consideration	Guideline justification: describes the types of knowledge expected to be presented and the applicability of recommendations based on the importance of condition at which is addressed
14	Methods Used to Search the Evidence	Specification by choosing from a predefined list the strategy used in searching the evidence (Hand-search of Published Medical Literature (Primary Sources); Hand-search of Published Medical Literature (Secondary Sources); Electronic Medical Databases; Searching the Unpublished Data)
15	Description of 14	Description of searching strategy with specification of the medical journals and databases included in strategy
16	Number of Source Documents	Specification the number of source documents consulted
17	Methods Used in Evidence Analysis Process	Specification by choosing from a predefined list the method or methods used in analysis of evidence: Decision Analysis; Meta-analysis; Systematic Review; etc.
18	Methods Used to Assess the Validity and Relevance of the Evidence	Specification by choosing from a predefined list the method or methods used in assessment of validity and relevance of evidence: Expert Consensus; Delphi Method Consensus; Subjective review; Weighting According with a Rating Schema
19	Description of 18th element	Description of the method(s) used in validity and relevance assessment of evidence
20	Methods Used to Formulate the Recommendations	Specifying by choosing from a predefined list (Informal Experts Consensus; Expert Consensus – different specified methods) the method used
21	Description of 20 element	Succinct presentation of method(s) used to formulate the recommendations
22	Recommendations	Succinct presentation of recommendations regarding the patient management. Where it is available, presentation of clinical algorithms
23	References Supporting the Recommendations	Lists the references (Vancouver style) of evidence supporting the recommendations
24	Potential Benefits	Description of the potential benefits associated with implementing the guideline recommendations (if it is available will be included the characteristics of the target population at which are obtained the best benefits)
25	Potential Harms	Description of the anticipated harms, potential risks or adverse consequences associated with the guideline's recommendations
26	Contraindications	Specification the instances which might render the use of medications or procedures improper, undesirable
27	Method of Guideline Validation	Specification of the methods used to validate the guideline by chousing the appropriate method(s) from a predefined list (Clinical Validation; Comparison with Guidelines from Other Groups; External or Internal Peer Review, etc.)
28	Description of 27th element	Concise description of the methods used for guideline validation
29	Implementation	Description of the implementation strategy
30	Specification of the Implementation Strategy	Captures the details of the method(s) used by the guideline developer to implement the guideline
31	References	Lists the references of guideline (Vancouver style)
32	Authors of the Guideline	Name and surname of the authors, scientific and didactic degree, institution, e-mail
33	Comments	Specification of the authors comments address to the guideline
34	Financial resources	Specification of the source(s) of financial support for guideline development
35	Conflicts of Interest	Identification the conflicts of interest if there are present
36	Copyright	Provide the copyright statement of the organization that submitted the guideline
37	Target Population	Description of the characteristics of target population
38	Age of the Target Population	Specification by choosing from a predefined list the age group(s) of the target
39	Sex of the Target Population	Classifies gender of the target population

GUIDELINE(ONLINE) application: development and implementation

The implementation of the GUIDELINE (ONLINE) system was performed by the use of MySQL database server [25] and PHP programming language [26]. The application used a MySQL database named `gpm`, which contains four master tables called `gmodels`, `models`, `guides` and `user` (which manage the model descriptions and the evidence-based guideline fields and their contents) and two secondary tables called `desc` and `dict` (which contains the MeSH descriptors used in indexing process).

The informatics system contain six modules (Guideline Create, Guideline New, Guideline Tree – display as a tree structure all guidelines stored by application, Guideline Display – display a choused evidence-based guideline,

Guideline Field – display the content of a specified guideline field, and Guideline Search – allow searching the guideline into the application) and theirs interfaces are sustained by a series of *.php programs.

Results

The GUIDELINE (ONLINE) application is an original one, developed after a comprehensive study of international and national specialty literature regarding the methodological approaches of clinical practice guideline. The application is hosted on AcademicDirect domain and is accessible at the following address:

http://vl.academicdirect.org/medical_informatics/guidelines/

The first window of the applications and its modeles are in figure 1.

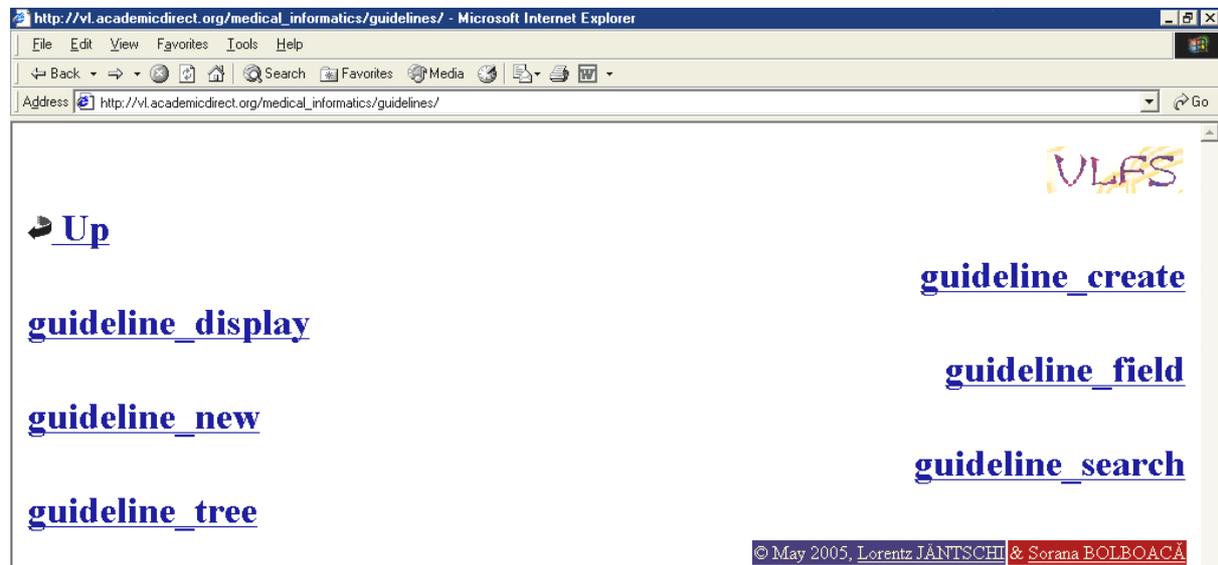


Figure 1. The GUIDELINE (ONLINE) application: first window

The guidelines create module assists the user in creation of a new standardized guideline. The feature is accessible just for the administrator of the database and allows:

- Specification of the abbreviation of the new guideline model (three letter);
- Specification of the name of the guideline model;
- Specification of the name of the guideline title of new model;
- A short description of the guideline model.

The administrator of the application has the right of inclusion into the databases of new models, and after the completion of the above-described field can be create and define as many fields as it considered opportune. The

description of each field is necessary in order to guide the users which create a new evidence-based guideline regarding to the type of information which can be include into a specific field.

The guideline new module assists the users in creation of new evidence-based guidelines based on standardized existent molel. The module has two major functions: assisting creation of new evidence-based guidelines and an assisting the users in chousing the correspondences between the information of a previous created guideline and its corresponding fields from the standardized structure.

The user must to make two steps in creation of a new evidence-based guideline. The

standardized evidence-based model is selected (figure 2) and the application assists the users in creation of a new evidence-based guideline

through guidance regarding the information that is necessary to be complete in each field (figure 3).



Figure 2. Interface of choosing the model

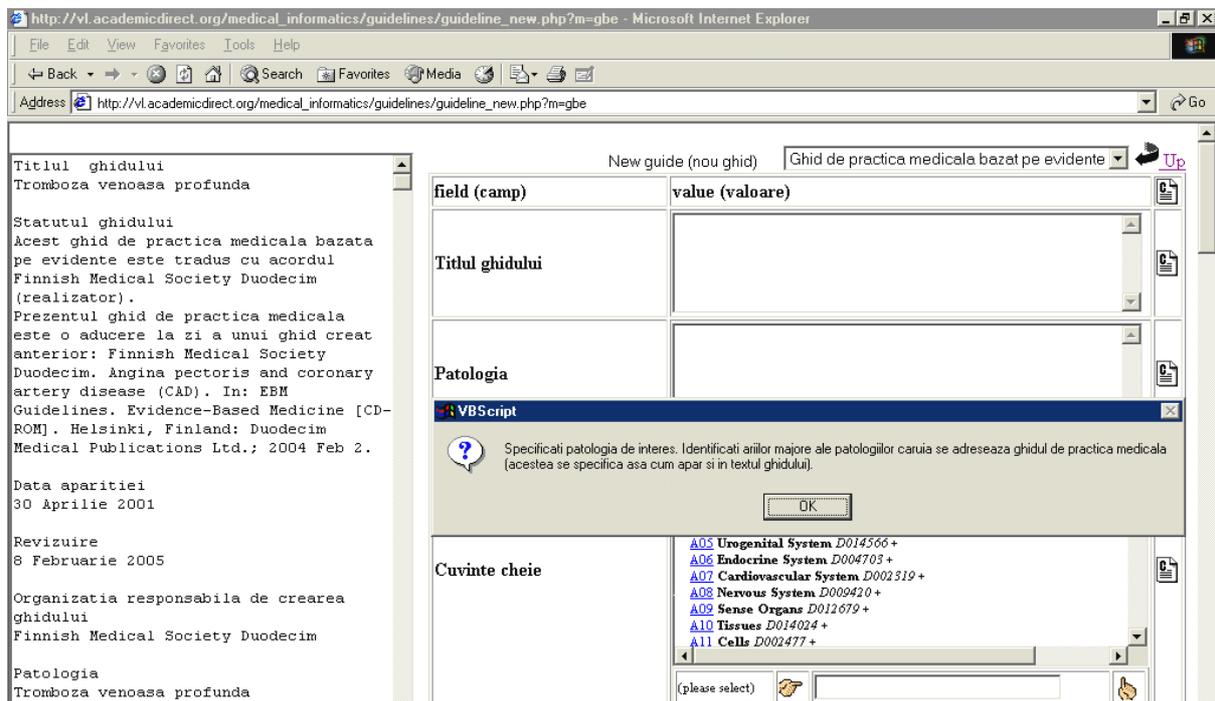


Figure 3. The interface of a new evidence-based guideline creation

There were created a series o buttoms with specific function in assisting creation of a new guideline, as follows:

- : display the informations regading at the kind of knowledge must be filling into a selected field;
- : allows after selection of the MeSH descriptor it inclusion into database;
- : allows deleting the MeSH descriptor or descriptors from the database;
- : allows to the user to delete the contents from the fields which allows selection of an option from a list.

The creation of a new evidence-based guideline can be performed by typing the information for each field; by selection and copy to clipboard

the information existing in a document and past it into the corresponding field; and by chousing the information from a predefined list (there were defined twelve fields which allow to the users to select the information).

After filling the information into the standardized model, the evidence-based guideline can be saving into the database by authorized users. A message of saving the data into the database informs the user that the guideline was saved.

Using the application into the training process is possible and allows to user to find the correspondace between the text and its corresponding field. The text can be selecte from the left-side window and by drag-and-drop can be inserting into the corresponding field in right-side window. Though the validation of the process by activatiog the Submit button from

the bottom of the window, the application display the rightness of the filling for each field (✓ sign if the information was correct and

✗ sign if the information was incorrect, see figure 4).

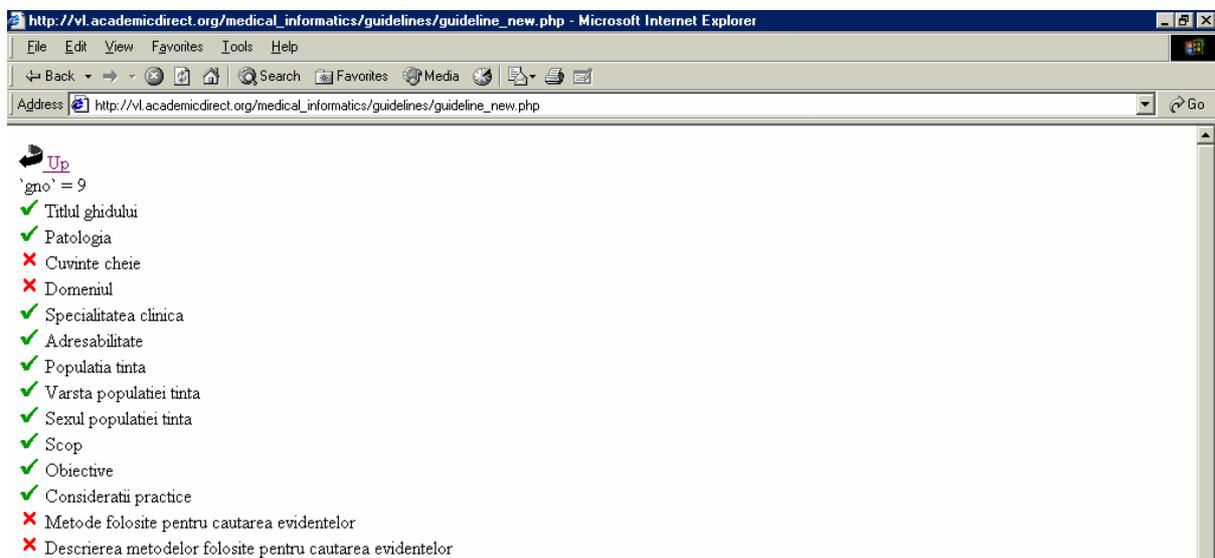


Figure 4. The displaying of the rightness of the guideline windows

The guideline field module allows to the user to display the information from a specified field. If we are interested to display the information of 'Potentiale efecte secundare ale aplicarii recomandarilor' (Potential Harms), in the address bar we will add the following

specification:
`?gno=9&field=Potentiale+efecte+secundare+ale+aplicarii+recomandarilor`. The application will display the request information as are presented in figure 5.

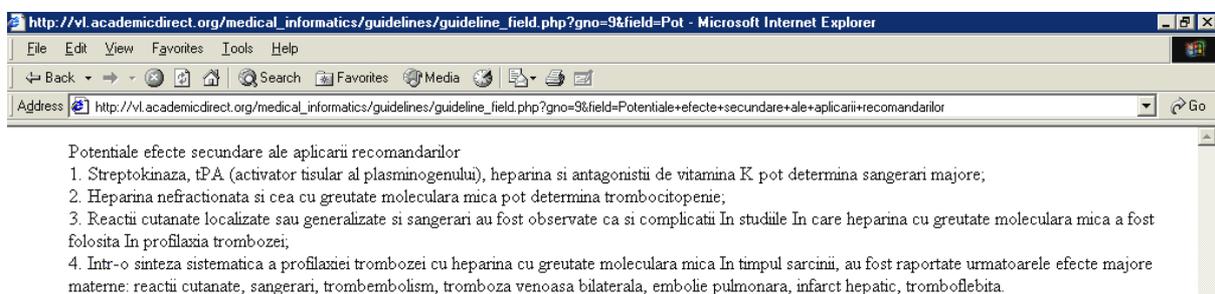


Figure 5. Displaying the information of a specified field

The guideline display module allows to vizualise the information of a choused evidence-based guideline (see figure 6.).

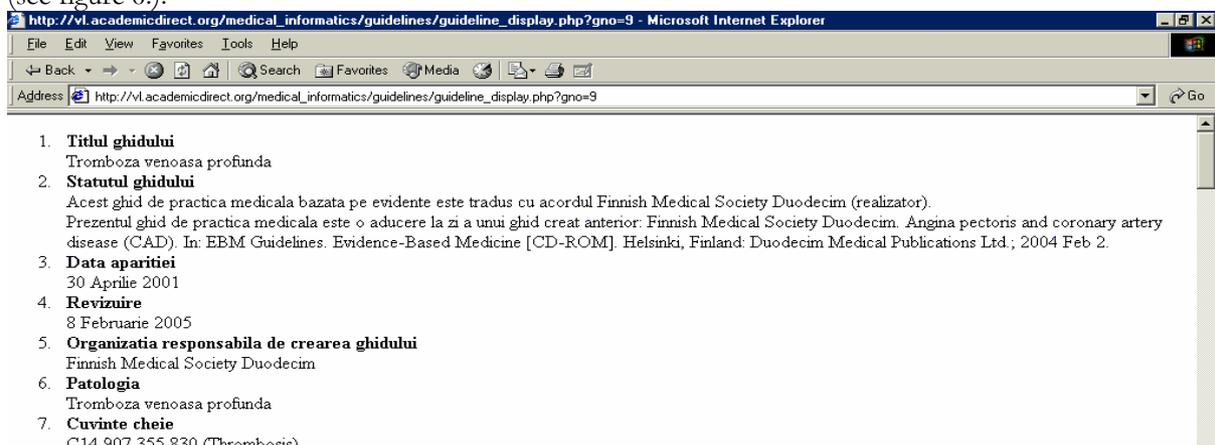


Figure 6. The display window

The displayed guideline can be print if we have a printer and/or can be save as *.html file (if we desire to show as in the Internet browser) or *.txt file.

The guideline search module allows to the user to search the database by specification of at least one out of five criterions (the guideline model, predefined fields, MeSH descriptor, the author,

and keywords; see figure 7). The search can be imposing to be narrow by selection of the 'strict' option or broad by selection of \forall button. Three out of five search criterions (model, field and authors) allows choosing the request information from a list of terms which correspond with the database recordings.

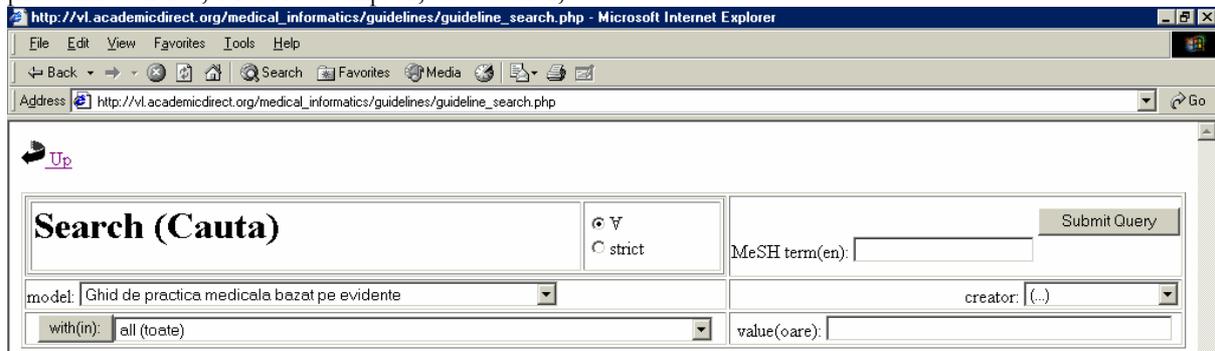


Figure 7. Search window

All guidelines stored by the application can be visualiz as a tree structure through the guideline tree module (see figure 8). The + sign

allows the extension of the visualization towards terminal branch while the – sign the stint of the branches.

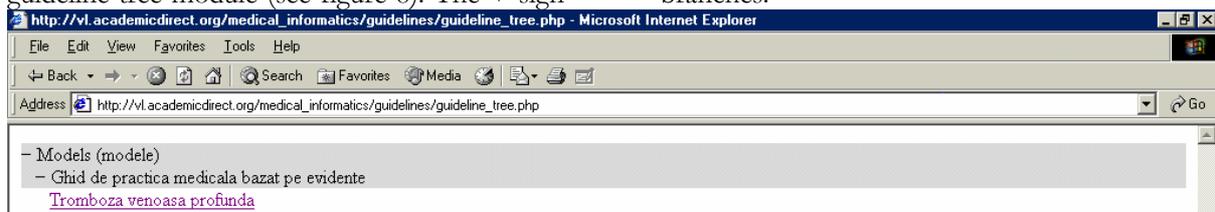


Figure 8. The window of the guideline tree module

Discussions

Created on an proper methodology, the GUIDELINE (ONLINE) application is a complex and unitary one and allows creation of standardized guideline models, assist the users in creation of evidence-based guidelines in native language by imposition of a structure and allows the management of the guideline, being the first application from this type in Romania.

The application is dignigy throuth its functions: creation of guideline model, creation assisted by computer of a new evidence-based guideline and management of guideline models and evidence-based guidelines.

The guideline model creation function can be use just by the users which have defined the rights of saving the information into the database. The application imposed to the user to define four characteristic of the new model (abbreviation, the name of the guideline, the name of the field which will store the guidelines title, and the description of the model)

The intended users of assisting creation of new evidence-based guidelines function are

medical professionals imply in creation of evidence-based guidelines and allows: assisting creation of a new evidence-based guideline based on the predefined model; choosing from the predefined list the proper options for specific fields; and saving the guideline into the database.

The intended users of the management of guideline models and evidence-based guidelines function are physicians, students, residents and any medical personal which are interested in evidence-based guideline. This function allows: filtering the GUIDELINE (ONLINE) database; displaying a specific guideline; printing and/or saving the evidence-based guideline of interest; searching by the content of a specified field and/or by guideline. Searching a guideline into the database can be made considering one or more than one out of five criterions, narrow or broad.

The features of the GUIDELINE (ONLINE) application are:

- Easy-to use: the application has a friendly interface and can be use by any person which

has minimum computer skills (starting-up a computer, Internet browsing, select, copy and paste information);

- Flexibility: once the standardized model was created its implementation is a facile process and its suiting in accordance with the diligence of the authors can be performed any time when it is considered opportune;
- Accessibility: the access to the application is not restricted by any time schedule but is accessible just if the user has a computer connected to the Internet;
- Multi-tasking: the application can be used simultaneously with other applications;
- Multi-users: the application can be used simultaneously by more than one user;
- Guidelines integrity: the information stored into evidence-based guidelines are protected against unauthorized modification through encrypted password.

The GUIDELINE(ONLINE) application can be used as an instrument of evidence-based guidelines dissemination, being useful in the process of implementation of guidelines at the health care system, an important facility of the application being the possibility of updating the guidelines information in real time and as many times as is considered opportune.

The utilization of the GUIDELINE (ONLINE) application is restricted just by the existence of a computer connected to the Internet and by the user's computer skills.

Comparing with the existing applications at the international level (National Guideline Clearing House [27], Guidelines Finder [28], Infobase [29], NICE Guidelines [30], EBM Guidelines [31], etc.) beside the visualization and search of the guidelines, the GUIDELINE(ONLINE) application offers to any nationality interested in creation of standardized guideline models a proper free-to-use environment.

The capitalization and future development schema of GUIDELINE (ONLINE) application include:

- Assisting the medical organizations and associations in implementation of standardized guideline models;
- Development of the database by sustaining creation of evidence-based guidelines;
- Development of a standardized structure useful in indexing the guidelines or

translation in Romanian language the MeSH descriptors with the approval of the authors.

It is well known that development of an application which allows assisting creation and management of standardized guideline models and clinical practice and/or evidence-based guidelines is not enough in their implementation at the level of health care system [32]. The GUIDELINE(ONLINE) application can be the first step in implementation of clinical practice guideline in Romanian health care system, offering to the Romanian Ministry of Health and to the Romanian College of Physicians an interactive environment useful in creation of guidelines and their management. In order to be used at its maximum capability, the application must be sustained by creation and implementation of a national deontological frame. Development of the application by creation of standardized models and evidence-based guidelines will make possible the dissemination of actual, valid and relevant evidence at the level of Romanian practitioners and through them the improvement of quality health care services.

The development of the GUIDELINE (ONLINE) APPLICATION PROVES that development of the standardized guideline models and evidence-based guidelines in native language is possible. These activities must be performed by specialized teams, by physicians with strong English knowledge, with ample expertise in health care, with proper abilities in searching the best available evidence and assessment of its validation and relevance, teams which to be able to integrate the best available evidence from the international level with Romanian values, and with national diagnostic, screening and therapeutic possibilities.

Conclusions

The GUIDELINE (ONLINE) application did not have as aim to impose the proposed evidence-based model; it is desired to attract the attention of the competent forums that the implementation of the standardized guideline models is possible and real in Romanian.

The application opens the pathway through creation of standardized guideline models and clinical practice guideline in native language.

References

- [1] Field M, Lohr KN. Attributes of good practice guidelines. In: Field M, Lohr KN, editors. *Clinical practice guidelines: directions for a new program*. Washington, DC: National Academy Press, 1990. pp. 53-77.
- [2] Woolf SH, Grol R, Hutchinson A, Eccles M, Grimshaw J. Clinical guidelines: potential benefits, limitations, and harms of clinical guidelines. *Br Med J* 1999;318:527-30.
- [3] Farquhar CM, Kofa EW, Slutsky JR. Clinicians' attitudes to clinical practice guidelines: a systematic review. *Med J Aust* 2002;177(9):502-6.
- [4] Fischer MA, Avorn J. Economic implications of evidence-based prescribing for hypertension: can better care cost less? *JAMA* 2004;291:1850-6.
- [5] Steinberg PE. Improving the Quality of Care — Can We Practice What We Preach? *The New England Journal of Medicine* 2003;348:2681-2683.
- [6] Ollenschläger G, Marshall C, Qureshi S, Rosenbrand K, Burgers J, Mäkelä M, Slutsky J. Improving the quality of health care: using international collaboration to inform guideline programmes by founding the Guidelines International Network (G-I-N). *Qual Saf Health Care* 2004;13:455-60.
- [7] Thomson R. Challenges for an international guidelines collaboration. *Qual Saf Health Care* 2004;13:409-10.
- [8] The AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. *Qual Saf Health Care* 2003;12:18-23.
- [9] Shekelle PG, Woolf SH, Eccles M, et al. Clinical guidelines: developing guidelines. *Br Med J* 1999;318:593-6.
- [10] Eccles M, Mason J, Freemantle N. Developing valid cost effectiveness guidelines: a methodological report from the north of England evidence based guideline development project. *Qual Health Care*. 2000;9:127-32.
- [11] Thomason M, Cluzeau F, Littlejohns P, Ollenschlaeger G, Grilli R, Rico-Iturrioz R et al. Guideline development in Europe: An international comparison. *Int J Technol Assess Health Care* 2000;16(4):1039-49.
- [12] Leslie LK, Weckerly J, Plemmons D, Landsverk J, Eastman S. Implementing the American Academy of Pediatrics attention-deficit/hyperactivity disorder diagnostic guidelines in primary care settings. *Pediatrics* 2004;114(1):129-40.
- [13] Kaiser R. Antiemetic guidelines: are they being used? *Lancet Oncol* 2005;6(8):622-5.
- [14] Haagen EC, Nelen WL, Hermens RP, Braat DD, Grol RP, Kremer JA. Barriers to physician adherence to a subfertility guideline. *Hum Reprod*. In press 2005
- [15] Smith L, Walker A, Gilhooly K. Clinical guidelines of depression: a qualitative study of GPs' views. *J Fam Pract*. 2004;53(7):556-61.
- [16] Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999;282:1458-1465.
- [17] Mol PG, Rutten WJ, Gans RO, Degener JE, Haaijer-Ruskamp FM. Adherence barriers to antimicrobial treatment guidelines in teaching hospital, the Netherlands. *Emerg Infect Dis* 2004;10(3):522-5.
- [18] Clarkson JE. Getting research into clinical practice - barriers and solutions. *Caries Res* 2004;38(3):321-4.
- [19] Kasje WN, Denig P, de Graeff PA, Haaijer-Ruskamp FM. Physicians' views on joint treatment guidelines for primary and secondary care. *Int J Qual Health Care* 2004;16:229-236.
- [20] Kasje WN, Denig P, Haaijer-Ruskamp FM. Specialists' expectations regarding joint treatment guidelines for primary and secondary care. *Int J Qual Health Care* 2002;14(6):509-18.
- [21] Summerskill WS, Pope C. 'I saw the panic rise in her eyes, and evidence-based medicine went out of the door.' An exploratory qualitative study of the barriers to secondary prevention in the management of coronary heart disease. *Fam Pract* 2002;19(6):605-10.
- [22] World Health Organization [home page on the Internet]. ©2005 [cited 2005 September]. Available from: <http://www.who.int/>
- [23] Wollersheim H, Burgers J, Grol R. Clinical guidelines to improve patient care. *Neth J Med* 2005;63:188-92.

[24] Ministerul Sănătății [home page on the Internet]. [cited 2005 September]. Available from: <http://www.ms.ro>

[25] MySQL [online]. ©1995-2005 [cited 2005 August]. Available from: URL: <http://www.mysql.com>.

[26] PHP [online]. The PHP Group; ©2001-2005 [cited 2005 August]. Available from: URL: <http://www.php.net>.

[27] National Guideline Clearing House [online database]. ©1998-2005 [cited 2005 September]; [about two screens]. Available from: URL: <http://www.guideline.gov>.

[28] Guidelines Finder [online]. © Crown Copyright [cited 2005 September]; [about one screen]. Available from: URL: <http://libraries.nelh.nhs.uk/guidelinesFinder>.

[29] Infobase - Clinical Practice Guidelines from the Canadian Medical Association

[online]. ©1995-2005, Canadian Medical Association [cited 2005 September] [about one screen]. Available from: URL: <http://mdm.ca/cpgsnew/cpgs/index.asp>.

[30] National Institute for Clinical Excellence (NICE) Guidelines [online]. ©2005 National Institute for Health and Clinical Excellence [cited 2005 September] [about two screens]. Available from: URL: <http://www.nice.org.uk>.

[31] Evidence-Based Medicine Guidelines [online]. [cited 2005 September] [about one screen]. Available from: URL: <http://www.ebm-guidelines.com>.

[32] Bergman DA. Evidence-based guidelines and critical pathways for quality improvement. *Pediatrics*. 1999;103:225-32.