Guideline Development: Focus on Breast Cancer Screening in the EsPeR Project

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Abstract

We describe in this paper, the implementation of a clinical practice guideline focused on breast cancer screening. Our aim in conceiving such a computerized guideline was first to help general practitioners in appreciating the risks their female patients might develop breast cancer and secondly to suggest them the screening measures adapted to each particular case. This implementation enables us to present our general methodology to elaborate and promulgate guidelines within the EsPeR project. This methodology aims at providing guidelines based on knowledge validated according to the EBM principles, that can be used in real time and updated according to current knowledge.

Keywords:
Practice Guidelines; Decision Making; Computer-Assisted Screening; Internet; Breast Cancer Screening; Risk.

Introduction

The steadily increasing volume of medical knowledge sets the problem of its effective integration within everyday practice. Guidelines can help practitioners find the appropriate care by providing validated, synthesized knowledge and presented in practical cases. However implementing these guidelines is not always efficient. Their efficient use in daily practice is conditioned to a great number of factors [1]. The impact of guidelines on clinical practice depends on the process of their development. Elaborating their content, promulgating and updating the guidelines are key steps to their effectiveness and to their effective use by practitioners.

Several methods can be applied to elaborating guidelines [2]. The ones using EBM (Evidence-Based Medicine) are in full expansion. These guidelines provide rigorously validated recommendations based on a relevant review of the literature. End users give full credit to such recommendations and therefore are more likely to adhere to them.

Although publishing guidelines in scientific journals is the standard means of dissemination, neither is their use convenient nor are they easily available. Furthermore, guidelines using this medium cannot easily be updated. The document has to be entirely republished (even for a minor change), penalizing the user owing to the piling up of documents and the delay in having access to the published updated guideline.

Guidelines databases, on specialized Web sites solve the problem of their accessibility and of their updating. However, the problem of their everyday use still remains [3]. The practitioner often has to read several pages in order to find the appropriate care for a specific clinical circumstance. The practitioner doesn't have time to refer to that form of information during the medical consultation. Using the guideline at the point of care should help the practitioner in pointing out some elements that may have been missed out by the usual questions to the patient.

The final objective of the EsPeR project (Personalized Risk Estimation) is to provide general practitioners with a web site specialized in the prevention of prevailing diseases among the French population and for which screening and/or prevention measures are proved to be useful and feasible. Part of this project focuses on setting up online tools that can estimate risks of morbidity and produce individualized recommendations in real time. To that end, our guidelines can be consulted from an application, which automates the collection and the inference of patient data.

We have in particular developed a guideline for breast cancer screening, as although there are efficient means of screening such a cancer, there are not always correctly used in daily practice [4]. Female breast cancer is a frequently occurring pathology. In France, it ranks first in terms of incidence and mortality [5]. The estimated probability for a woman to have a breast cancer before the age of 75 is close to 10% [5]. However mortality does not increase at the same rate as incidence, which shows that screening is improving (in terms of estimating risks and early diagnosis) and so is the efficiency of the therapy.
The risk of having breast cancer can be expressed by using conditional probabilities or risk levels. In the first case, the objective is to estimate the probability that a woman aged \( x \) might develop a breast cancer within a \( n \) future, knowing that she doesn't have breast cancer at the given age. Some authors have elaborated such risk calculating equations. Gail's model [6] has probably been the most commonly described. In the second case, risk levels are determined by relative risks taken from the literature (Taplin et al. [7] for example). According to such factors of risk, a woman can know her own risk level of having a breast cancer and the recommendations adapted to that specific level.

**Methods**

**General cyclic process of elaboration**

We use a cyclic process to elaborate our guidelines. This process, which has previously been described by Zielstorff [8], enables us to update and complete the guidelines according to current knowledge and measure their effectiveness among end users.

The process starts with the definition of the guidelines objectives. In this particular case, it specifies the screening methodology adapted to the risk for a woman to have a breast cancer. A relevant review of the literature, added to experts' point of views is necessary in order to collect and synthesize knowledge on the subject. Evaluating the level of evidence of such knowledge leads to elaborating the content of the guideline. The following step consists of writing the guideline. The text must be clear and never ambiguous. It is used to draw up a decision tree where the sequence of logical conditions leads to a recommendation. These conditions concern the factors of risks of breast cancer.

The decision tree is used to implement the guideline in an algorithm and to diffuse it on the web site through an interactive program. The program questions the user in order to collect the patient data that are necessary to estimate the level of risk. It automatically infers these data and displays a personalized recommendation.

The next step evaluates the efficiency and the ergonomics of the system among a panel of general practitioners. It is supplemented with a watch of all publications on the subject so as to find all new information on breast cancer. The steps of elaboration, writing and dissemination are then once again implemented having taken into account the precedent results.

**Guidelines knowledge**

Our process of elaborating recommendations (figure 1) is based on EBM rules to measure the quality of the methodology and the level of evidence of scientific information. Personalized estimation of the risk and recommendation given to the practitioner are formalized by evidence levels and recommendation grading as they have been defined by the Oxford Center for EBM [9].

![Figure 1 – Process of elaborating the contents of guidelines](image)

Once having defined the factors of risks, we fix homogenous levels of risk that assemble different subgroups of subjects whose characteristics form a separate entity. We then identify the screening measures and we elaborate a personalized recommendation for each subgroup of patients. We work with experts in breast oncology who validate and/or reevaluate each of these steps.

**Online implementation**

One of the priorities within the EsPeR project is to display guidelines that can be used by the practitioner in real time (i.e. in front of her patient). The practitioner must quickly obtain appropriate recommendations adapted to the patient's profile. We have realized a program based on the specifications of the GLIF model (GuideLine Interchange Format) [10]. This object-oriented model uses the elements common to four American decision making systems and has some similarities with the model that stems from European projects [11].

GLIF determines a group of classes which enables us to represent a guideline in the form of an algorithm. A guideline is regarded as a sequence of steps; it specifies the actions that have to be performed and the conditions that need evaluation before obtaining a recommendation. The steps of the algorithm, the patient data as well as the recommendations can all be connected to sources of information. We take advantage of this connection to offer the user supplementary information if needed.

GLIF is independent of the implementation language and quite easy to use. However we have extended certain classes of the GLIF model in order to be able to represent complex patient data and to specify the actions that the program performs. For instance, in the case of breast cancer we had
to build data such as family history into the model. We have decided to represent that type of data as an aggregate of property-value pairs. In our model a family history of breast cancer is defined as an object which has three properties: the degree of relations, the age of the patient when the pathology was first detected and the laterality of the lesion.

In order to optimize the actions that the program performs we have created specific classes: some of them specialize in the questioning and the updating of the patient database on the EsPeR web site whereas others are in charge of questioning the user, and of displaying recommendations. All the classes that have been created inherit the specifications of the GLIF model. This enables us to develop interactive guidelines which use complex well documented knowledge, integrated to other services which the EsPeR web site offers.

Results

EsPeR architecture: position of the guideline module

The EsPeR sever is based on the architecture shown on figure 2. JDBC-ODBC, ASP (Active Server Page) from Microsoft™ and Java applets are all technologies used to communicate between the three levels.

The guidelines module (on the middle level) is implemented in Java classes. It has three complementary functionalities, sequentially executed:

- Collecting data from the online patient record made up by the practitioner on the EsPeR site. This patient record enables the practitioner to keep anonymous information therefore the same data won’t need a new capture during the next consultation. The module generates a form to be filled in when a patient datum is missing;
- Inferring patient data with the JRules engine provided by the ILOG™ company [12]. Rules are written in a classic form: IF <condition> THEN <action>
- Displaying a personalized recommendation on an HTML page.

Example

Scenario: Mrs. Durand, 47 years old, is consulting her general practitioner because her aunt has recently died of a breast cancer. She is worried and wonders if she shouldn’t be under close medical follow-up. After a thorough clinical examination no breast anomaly has been detected. The general practitioner then consults the EsPeR web site questioning the patient more precisely at the same time.

With the help of the personalized estimation of death probabilities [13], also accessible on the site, the general practitioner notices that the most probable cause of Mrs. Durand’s possible death within the next 5 to 10 years would be breast cancer. A hypertext link indicates that the practitioner can obtain a personalized risk estimation of breast cancer as well as recommendations screening. By clicking on this link he will activate the guidelines module on breast cancer, which will display a summary of previously recorded data on his patient (age, sex, addiction to smoking, blood pressure…). By clicking on the button “get a recommendation”, the practitioner is then guided by the program with the questioning of Mrs. Durand: he has to capture precise information about her personal and family history of breast cancer and ovary cancer; about any previous breast biopsy and its pathology result.

Each capture is followed by a data inference: the module checks if the information given is necessary and sufficient to stop the process and obtain a recommendation. The program quickly gives a recommendation adapted to the profile of Mrs. Durand. The system points out that there are minor risks of breast cancer in the case of Mrs. Durand and recommends a clinical follow-up and mammography every 12 to 18 months. It also gives a summary of data necessary and sufficient to the recommendation (figure 3).

The practitioner has access to further information through the hypertext links:
• "Grade B" link indicates the level of evidence of the recommendation and leads to a new window where this level is clearly defined (figure 4).

• The link "For further information..." gives access to precision about recommendation and on the bibliographic sources that have been used for its elaboration.

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Grade of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Large randomized comparative trials with indisputable results</td>
</tr>
<tr>
<td></td>
<td>Meta-analysis</td>
</tr>
<tr>
<td></td>
<td>Decision analysis</td>
</tr>
<tr>
<td>II</td>
<td>Small randomized comparative trials and uncertain results</td>
</tr>
<tr>
<td>III</td>
<td>Non-randomized comparative prospective trials</td>
</tr>
<tr>
<td></td>
<td>Cohort studies</td>
</tr>
<tr>
<td>IV</td>
<td>Non-randomized comparative retrospective trials</td>
</tr>
<tr>
<td></td>
<td>Case-control studies</td>
</tr>
<tr>
<td>V</td>
<td>No group-control, case-series report</td>
</tr>
</tbody>
</table>

The proposed recommendations tally with a strong professional agreement in absence of level of evidence

Figure 4 – Level of evidence and grade of recommendation

Discussion

There are two key points to an efficient prevention or screening strategy: a correct appreciation of the risk and good information on the means of prevention and screening. This strategy is not a static process: it evolves according to recent scientific research findings. The specific guidelines bring help to the practitioner, as long as there are available on an easily usable medium.

The EsPeR project aims at improving the prevention of the most prevailing diseases among the French population. It is based on putting validated medical knowledge at the practitioners' disposal for their everyday practice.

Predicting the risk of developing a breast cancer

It is essential to appreciate the risk that an individual might develop a breast cancer. According to such a risk, a recommendation is suggested.

Although a probabilistic model of risk prediction exists, Gail’s model [6], we have chosen a method based on building up homogenous risk levels. Indeed Gail's model has been developed in the USA on a population of white women aged from 35 to 79. It has been proved that the model overestimated from 30 to 50% the absolute risk of breast cancer [14-16]; especially among pre-menopausal women who did not take part to screening campaigns. Studies on the validity of the model were carried out on North-American populations; it would be hazardous to try to transpose them to French population. Finally, are there different screening measures for a woman whose risk in the next 10 years is of 29%, compared to another one with a 34% risk?

Elaborating recommendations

The analysis of the literature alone is rarely sufficient to elaborate a guideline where all clinical circumstances must be envisaged [17]. The point of view of experts add up to the analysis so as to make up for the possible lack of significant facts and to take into account the constraints of daily practice. In order to enable practitioners using our site, to appreciate the level of evidence of our recommendations, we always indicate it as well as the sources of information.

Guidelines diffusion

Usual media such as written texts or static web pages are not adapted to the use of guidelines in real time. When consulting such guidelines, the practitioner must read several pages to find the information that applies to his patient's case.

In the EsPeR project we have chosen an interactive promulgation of personalized instantiation of guidelines. Automating the collection of significant patient data reduces the time needed to consult the guideline. These data can be kept in an online patient record and therefore avoid redundant data capture for the same patient. In the breast cancer guideline, relevant data capture is done step by step. Data are required only if compared to those already known, they might modify the final recommendation. For example, if in the family history of a patient there has been more then three cases of breast cancers, a close follow-up must be recommended whatever other factors of risk may be detected (late pregnancy, nulliparity, biopsy of breast lesion in personal history...).

The recommendations are displayed in the form of succinct and specific texts. To avoid overloading the recommendation with information [18] we use hypertexts links. They give access to the bibliographic references that have been used and to a didactic page with information for interpreting levels of evidence.

Our model of guidelines is largely inspired by the GLIF model 2.0 [10]. The GLIF model can represent the logical content of a guideline but is less explicit about representing medical concepts and additional information (date of revision, type of guideline, evidence grading...). The research work of Schiffman et al. [19] and the new specifications of GLIF 3.0 [20] will be considered in our process of guideline elaboration.

Evaluation

Evaluating the EsPeR project is in process. At this first stage a panel of general practitioners are testing the web site during their consultation. The objective is to optimize the user interface and to detect any technical and/or cultural problems that might put obstacles to generalizing the use of the server.

In a second phase we plan to deal with the difficult problem of measuring the impact of the services offered by EsPeR on the practitioners behavior: how does the consultation of
the site and especially the guidelines modify practitioners behavior with female patients?

Members of the EsPeR project


Acknowledgements

The development of the EsPeR project was possible thanks to a grant from the “Caisse Nationale d’Assurance Maladie des Professions Indépendantes”, Paris (CANAM)

References


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